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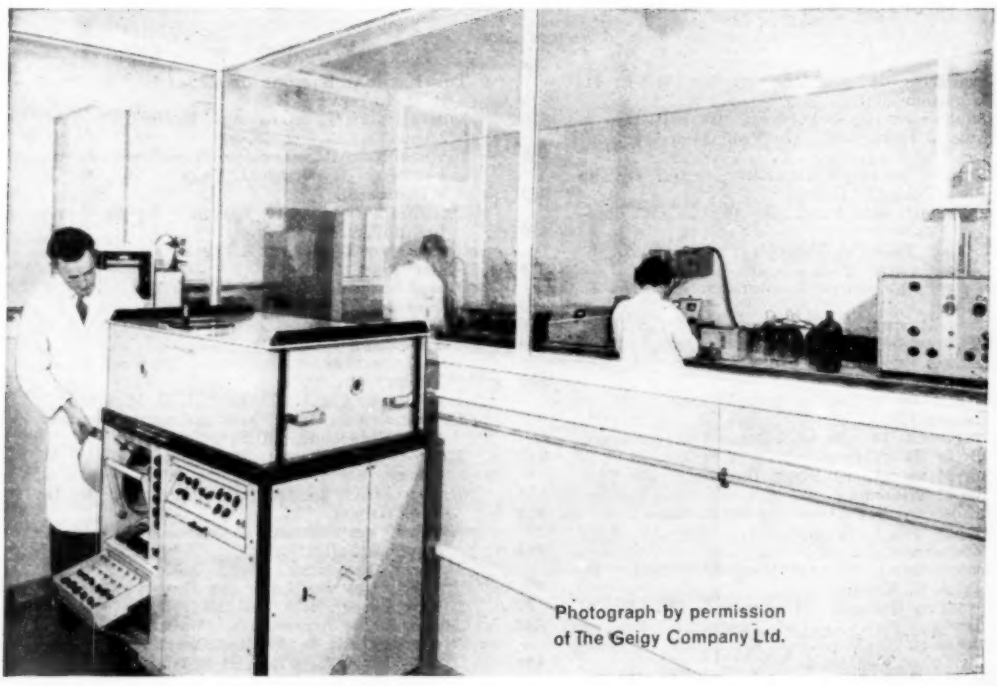

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CO-OPERATION IN RESEARCH

IT is something more than mere coincidence that Dr. B. V. Bowden, in a discourse at the British Association at Norwich last September on the impact of automation, should have urged not simply the wider and more imaginative use of the electronic computer but also pointed to the implications of such developments for university and technological education. In fact, the position of the universities in this field has been the subject of special comment in the general survey from the University Grants Committee which this year accompanies the usual returns from universities and university colleges in receipt of a Treasury grant. Furthermore, in the June 1961 issue of *Vestes*, the Australian universities review, J. M. Bennett describes the university computing centre in Australia, where three such centres have been operating since 1956. Again, the current issue of *Impact* includes a paper by Prof. R. Courant which, while discussing general problems confronting computing centres, emphasizes particularly the major effort required, especially in universities, to train a generation of scientists eager and competent to make full use of computers as scientific tools—an effort which requires the breaking down of departmental boundary lines and as such may involve changes in departmental organization, as well as co-operation on a broad scale with industrial research organizations. A recent article by Dr. R. C. Campbell in *Chemistry and Industry* (p. 1786, November 4), on the administrative uses of a computer in a university, points to some interesting possibilities in the use of computers and indicates an encouraging prospect for such developments.

Mr. Bennett, who notes that more than 3,000 automatic digital computers are now in service throughout the world and that more than 100 are in service in universities in the United States, while nine British universities have computing centres, considers not merely the man-power required to operate computers and to utilize them, but equally the problems of finance and administration. The university computing centres in the United Kingdom are financed largely from public funds through the University Grants Committee as a result of an agreement reached with the Treasury in 1954. Grants amounting to £381,000, out of the total university expenditure of £417,000, were eventually made for the purchase of computers and ancillary equipment on the recommendation of the University Grants Committee, advised by the Advisory Committee on High-Speed Calculating Machines of the Department of Scientific and Industrial Research. The initial allocation was primarily on a regional basis. At that time, Cambridge already possessed a computer and Sheffield was able to make very favourable arrangements for hiring computer time. Accordingly, Durham, Leeds, London, Manchester, Oxford, Southampton and Glasgow received computers, and eventually Liverpool purchased a computer, partly from industrial contributions and partly from its own resources.

In 1957, an Inter-University Committee on Computing was established, under the chairmanship first of Prof. D. R. Hartree and later of Sir Willis Jackson, to advise the Committee of Vice-Chancellors and Principals on policy questions and to promote co-operation in this field between the user universities and between universities and other bodies. In 1959 this Committee, in its first report, emphasized the rapid expansion of university work, which had been under-estimated and was steadily squeezing out extra-mural work, and recommended further extension of computing facilities in the universities. As a result, the University Grants Committee agreed, in October 1959, to consider a further allocation of computers to the universities in Britain. When approached, twenty-two universities, including all but one of the universities already possessing a computer, replied that they wished to apply for a new machine.

Two universities applied for *Atlas* computers and the University Grants Committee took the view that provision of machines costing £1·5–£3 million each was a question to be handled on a national basis, and accordingly the claims of these two universities and of other institutions for *Atlas* facilities have been assessed by a working party under the Minister for Science. As a result of this survey, the Government has placed an order for such a computer to be installed at Harwell under the auspices of the National Institute for Research in Nuclear Science, and it is assumed that these facilities will be available to those universities which need them. The University of Manchester, by its own special arrangement with the makers, will possess an *Atlas* computer which will be available to certain other universities.

As regards the medium-sized computers, the University Grants Committee appointed a small subcommittee, under the chairmanship of Sir Willis Jackson, to give detailed consideration of the types of machine required by the universities, to questions of timing and priorities, and to the use that might be made of the older displaced machines. This subcommittee included representatives of the Department of Scientific and Industrial Research and the Ministry of Education, and had the assistance of Dr. Howlett, of the Computing Department of the Atomic Energy Research Establishment; its advice was accepted by the University Grants Committee, which in March 1961 sought authority from the Chancellor of the Exchequer for a programme to provide medium-sized computers, involving expenditure of about £2 million, between 1961 and 1965. This authority has been given, and accordingly twenty-one universities are expected to have their own computer facilities, while the remaining universities have access to others.

This, however, is only a particular aspect of the relations between the universities and the Government in Britain, or indeed of university expenditure on research; but it is of special interest in view of Lord Hailsham's remarks about those relations in his recent addresses on science and government in a free society (see *Nature*, November 4, p. 393, and p. 787 of this issue). Lord Hailsham did not suggest that the British system, which, in effect, allows Government funds to be administered by the universities themselves, is the only possible way of ensuring adequate Government support for university research without infringing academic freedom, but he did claim that the system works, and his addresses make very plain the dangers which attend the creation of separate Government-sponsored institutes and generally the separation of research and teaching. He was emphatic that the most advanced scientific work should be located in or near the universities, where this is possible, or directed by university personnel.

In his earlier address, Lord Hailsham was concerned with maintaining a healthy balance between research and teaching, between Government research and that proceeding in the universities and in industry, between pure and applied research and development work, and he was no less conscious of the growing opportunities for international co-operation in research. It is with the balance between research and teaching that the University Grants Committee is concerned, and at the request of the Advisory Council on Scientific Policy it has made a further estimate of the resources in the universities which are devoted to research in the pure and applied sciences, medicine, dentistry, agriculture, forestry and veterinary science. Although it wishes to have further information of the numbers of technicians engaged in the various departments in the universities, since this matter, which has an important bearing on the effective use of research workers, is one to which the Committee is paying special attention in assessing the financial needs of the universities for the next quinquennium, the results of this survey are given in the Committee's general survey attached to the latest *Returns**.

The survey covered 16,882 university staff and research students, of whom 53 per cent were in the pure sciences (mainly physical) and 19 per cent in the applied sciences. Medicine (3,324), chemistry (3,013), engineering (2,445) and physics (1,909) claimed the largest numbers. Of the total, 7,522 were research students, and the proportion of research students to university staff varied from 2·0 : 1 in chemistry to 0·2 : 1 in medicine and dentistry. About 49 per cent of the time of staff and research students is estimated as devoted to research, varying from as little as 21 per cent in dentistry to 57 per cent in zoology. The total of 8,534 technicians included 563 chief technicians, 1,365 senior technicians, and 2,475 technicians; and on an average, there was one technician per member of staff and one to 1 : 1·8 members of staff and research students, the ratio varying greatly between subjects. Many of the technicians, moreover, had duties connected with teaching as well as with research, and a comparison with the figure for research laboratories in other institutions suggests that the ratio of technicians to research workers in the universities in Britain is below that necessary to ensure that the time of research workers is used most economically.

The University Grants Committee may well be understating the need, but it is satisfactory to note that it proposes to give special attention to this factor in its current assessment of the needs of the universities. On the expenditure side, the survey estimates that of departmental expenditure totalling £28·3 million, and including academic salaries, wages, departmental and laboratory maintenance and other like items, £14·1 million is attributable to research. If, further, it is assumed that some two-thirds of such 'overhead' expenditure as administration, libraries, maintenance of premises and the like applies to the sciences and applied sciences, and half of this two-thirds is attributed to research, the total rises to £18·3 million. To make this figure comparable with the total of £22 million quoted for the year 1958–59 by the Advisory Council on Scientific Policy in its report for 1959–60, there must be added a proportion for non-recurrent grants for building and equipment. For 1959–60 these grants amounted to £4·2 million, and if account is taken also of awards to research students which do not pass through the university accounts—and these are assumed to be worth on average £470 a year each—a further £3·4 million should be added, bringing the total to £25·9 million, which would represent some £2,140 for each research worker per annum, departmental expenditure alone amounting to £1,666, of which about £865 represents salaries of university staff. It is not clear, however, whether the figure of £25·9 million includes all the sums for research at universities which are made available through the Council for Scientific and Industrial Research and the Research Councils; but the figure compares with £23·3 million for research and development carried out by the universities quoted by the Advisory Council on Scientific Policy in the current report. Sir Harry Melville put the contribution from the Department of Scientific and Industrial Research in research grants and post-graduate studentships at more than £2·5 million in the past financial year.

The distribution of this research effort in the different groups of sciences varies from 38·3 per cent of man-power and 32·8 per cent of expenditure in the physical sciences to 1·8 per cent of man-power and 1·7 per cent of expenditure in dentistry: for the biological sciences the corresponding figures are 9·8 and 10·0; for the applied sciences, 19·1 and 18·0; for medicine, 19·7 and 27·2; and for agriculture, forestry and veterinary science, 5·9 and 6·6.

The University Grants Committee quite rightly once again urges that too great a significance should not be attached to many of the differences in research effort between subjects. Obviously, some regard

* University Grants Committee. Returns from Universities and University Colleges in receipt of Treasury Grant, Academic Year 1959–60. Pp. 76. (Cmnd. 1489.) (London: H.M.S.O., 1961.) 4s. 6d. net.

must be had to personal idiosyncrasies and abilities, and the research effort made in any one subject will undoubtedly vary from time to time, depending on such factors as the presence of an outstanding worker in a subject and the level of interest. In fact, the interest now being taken in the balance of research effort in Britain arises essentially from two roots: the need to see that in the universities and elsewhere the resources at the disposal of the research worker are such that he can make effective use of his time and of the costly equipment that is now so often required; and secondly, to ensure that there is a reasonable balance of research effort between the universities and other research institutions, Government or independent, between pure and applied research and development, as well as between subjects. It is only on such a basis that it is possible to plan a reasonable allocation of the limited resources in Great Britain and to press the claims of a particular research effort in the face of conflicting claims.

Lord Hailsham's recent addresses show that he is well aware of the problems involved, and alive to the dangers either of parsimony or of interfering with the universities' choice of projects or disposition of their resources. Inevitably, co-operation involves compromise and adjustment as between universities and other institutions, or between Government departments, industry and the universities; and the development of university co-operation in the use of computers, radio telescopes and cyclotrons, quite apart from the growth of international co-operation in research, will accentuate the need for further collaboration. At the present moment, when the University Grants Committee is formulating its proposals for the next quinquennium under the shadow of the Chancellor of the Exchequer's call for economy and reduction in public expenditure, a heavy responsibility rests on the Minister for Science to see that there is no retraction of the universities' research effort, either in respect of its contribution to the advancement of knowledge or to the training of man-power for research. The University Grants Committee, from its general review, appears to be taking the right measures to ensure the elimination of waste and the effective disposition of whatever resources may be made available. It is for the Minister for Science to satisfy himself that the resources put at the disposal of the universities are indeed adequate for the purpose, having regard to the nation's need for trained man-power, its total research effort in industry and Government institutions as well as in the independent research institutions, and to the possibilities of co-operation both on the national and on the international scale. In that task, moreover, he should derive powerful support from the recent report of Lord Plowden's committee in opposing any policy that would tend to apply 'start and stop' to research projects. Lastly, in a time of financial stringency, the Minister for Science might be specially watchful to see that no measures are introduced which hinder that invaluable movement and interchange of personnel between institutions or the regular exchange of ideas on which he himself has rightly placed much stress.

RESEARCH IN THE UNIVERSITIES*

By The Right Hon. VISCOUNT HAILSHAM, P.C.

Lord President of Council and Minister for Science

THE Rector of Imperial College has reminded me that it is a hundred years since the death of its founder, the Prince Consort, a man of vision and prescience who saw clearly, in an age only partially awakened to such things, the revolutionary changes for good which might be made in the conditions of human life by an unfolding scientific technology, imaginatively applied in a spirit of serious good will. In the bright light of mid-Victorian optimism, of which Prince Albert was in part an example and in part an initiator, much that has happened since would have seemed a perversion of those eager hopes. But enough has taken place to make sure that they were not altogether misplaced and to give us confidence that in their future realization the College which he founded will continue to play a noble part.

When writing of the first professorial unit in the College, Prince Albert described this part as having raised the new College to "a high pitch of usefulness and popularity". Usefulness and popularity are not always co-existent; but they are no bad things, provided they are kept in just the right balance with one another, and this, I believe, is what Imperial College has done.

The Rector also suggested to me, as a main topic for discussion, the subject of research in the universities —a theme particularly suitable in view of the strong tradition of research in Imperial College, and the important part which this tradition plays not only within the College but also in the scientific, technological and industrial life of the country as a whole.

This subject contains a clue to the whole development of an integrated modern culture on one hand, and of an adequate technology on the other; at the same time it is, as I shall seek to show, a matter of extreme complexity on which we have not yet discovered all the answers.

Can we begin without some idea of the kind of thing we want our universities to be, and the kind of purposes we want them to serve? For myself I cannot, and at the risk of exceeding my mandate I must deliver my testament of faith on this topic.

The eternal struggle of humanity is to reconcile freedom with authority, individual self-expression with the requirements of society. There have been many definitions of freedom, ranging from national independence to freedom of worship, from universal

*Substance of the Commemoration Day Address at the Imperial College of Science and Technology, delivered in the Royal Albert Hall, London, on October 26.

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suffrage to full employment, from social security to private enterprise. As a lawyer, as a politician, as a moralist, I have discussed them all, and admit that all have a certain contingent value. As a philosopher I have found them all inadequate. None of them by itself is intellectually satisfying.

I suspect that one reason for this is that, whatever it means, freedom cannot be seen in isolation from the search for the just and the true, the beautiful and the good—the ultimate values which men place on their existence. In their origins in the ancient world, the universities were the places where this search was correlated and discussed; and the academic freedom of the universities themselves, their intellectual stature, their moral quality, seem to me to be matters of immense importance, theoretical not less than practical, in the discussion of the relative values of tyranny and freedom, of democracy and authority, of law and morality. But if this is so, it is at least surprising that this is a matter which is almost never mentioned by the political theorists and lawyers who indulge in most of the arguments.

But if a unity of purpose, an integrated understanding of man and his environment, is not to be found in the universities, it will not be found in the nation, or in the world. This is dimly apprehended even by the multitude, even by the popular press when they pay sometimes disproportionate attention to the strange actions of undergraduates—or to the even stranger opinions of professors. But in terms it is almost never said. Yet the university world is the true melting-pot of society, the one great mixer where class distinctions are being abolished before our eyes, the one aristocracy of merit divorced from privilege, the one democracy where equality of opportunity is not confused with equality of achievement, reward or esteem. In the humanities it is generally accepted that, at this level, teaching and research cannot wholly be separated. My thesis to-day is that teaching and research in science must similarly be allied.

Yet side by side with their function as the teachers of human society as a whole, the universities have also the task of providing vocational training. It is idle to disregard or minimize this aspect of their activities —although many academics are far too fastidious to speak of it openly, and sometimes write letters to the papers decrying its discussion. The ugly truth is that if it had not been for this function, the universities would have neither been brought into being nor survived. If the Church had not needed educated priests, if the State had not needed educated administrators, if industry had not needed educated executives and technologists, there would have been no universities; and although medicine and law and the engineering professions, at least in Great Britain, have contrived partly independent systems, I doubt myself whether even these would survive—or maintain adequate standards—without a parallel system of academic courses to give them intellectual body.

But the truth is that the two functions are not independent of one another. Even on the vocational plane, teaching of the order we require for our administrative, our scientific and industrial leaders cannot be wholly divorced from research—the true pioneering of knowledge of all kinds. Research will tend to become barren and research workers to die out if attempts are made to divorce it from teaching.

But how is research to be financed? Who is to call the tune? And if the tune is to be called by the spirit of research itself, the λόγος as Plato puts it, carrying us along like the wind, What conceivable motive will be his who pays the piper?

The issue of academic freedom has never been very far below the surface of political life. At the time of the Reformation, and the Civil War, the questions were obvious. But in recent years, and certainly until 1939, they were scarcely asked. No one grudged the Prime Minister the right to nominate Regius professors; and academic resources depended as much on fees, endowments and donations as on public funds.

But by 1946 it was apparent that the scale of expansion forced on the universities by the range and rapid development of modern knowledge, and the insatiable appetite of industrial society for trained graduates, made it necessary that from henceforth the main patron of the universities would be the State. Happily to hand was the appointed instrument of State and university—the University Grants Committee, brought into being in 1919. I would think that on the whole this has managed to the general satisfaction to administer public generosity without corrupting academic freedom.

In one direction, however, the University Grants Committee has required supplementation. Built into university life is an innate conservatism—no bad quality, this, but one that needs to be balanced. From their start, the Research Councils—by which I mean the Department of Scientific and Industrial Research, the Medical Research Council, the Agricultural Research Council, and the Nature Conservancy —have encouraged the initiation of new projects of research, and particularly in relation to medical research have founded whole teams of research workers within, but not necessarily as integral parts of, the universities: and in the past four years the total value of the research grants given to universities each year by the largest of these patrons—the Department of Scientific and Industrial Research—has increased three-fold. I am rather proud that this has happened entirely within my own period of office, since I regard the development as wholly to the good.

For a second function of the universities—to initiate new studies, to fill in gaps in the old, needs (as no one knew better than Prince Albert) a living patron, something more adventurous, and perhaps a little more selective, than in the nature of things the University Grants Committee can be expected to be. The present size of the Government-sponsored research in the universities is, however, such as to give rise to new questions—both for the Research Councils and, I would say, also for the universities—which it will be my business and that of my successors in office to investigate in the coming months and years. Speaking broadly, it will be necessary to keep in mind the respective functions of the University Grants Committee and the Research Councils. But, at this stage, I would only mention, in passing, two small points.

First, the permanent structure of the universities is clearly a matter for the universities themselves, and the University Grants Committee is the constitutional channel for Government funds. It is vital to remember that the Research Councils' function is not to finance science in the universities as a whole, but to provide funds for new developments in research which cannot be adequately dealt with within the framework of the quinquennial system. But at what stage, and by what mechanism, can work originally fostered by the Research Councils be handed over—and how is the hand-over to be recon-

ciled with the academic law of the Medes and Persians against ear-marked grants ?

Secondly, a similar question, though not entirely limited to research, arises in relation to laboratory technicians and assistants—whose activities form an indispensable part of virtually all scientific work in universities. It is not my function, or that of the Research Councils, to provide part of the permanent staff of universities. The University Grants Committee rightly adheres to its policy of refusing ear-marked grants. This is a minor problem and can be solved within the university framework.

Since I first assumed Ministerial responsibility for the Research Councils, university research has been affected by a number of changes—changes both in scale and in character—in the field of scientific research generally. For one thing, in an increasingly wide range of disciplines the tools of research have become machines—and machines each of which is a major engineering project constituting a significant item in the capital investment programme. Apart from the big machines, the accelerators, the Jodrell Banks, the gas-bubble chambers, there is the problem of the new institutions, sometimes clustering around the facilities of a parent body, like the National Institute for Research in Nuclear Science round Harwell, yet half resenting and half resented by the parent organization which gave it birth.

Closely related to the machines, but potentially larger still, are newly emerging fields of investigation, too big, almost from the first, for association with teaching universities; too big, almost from the first, for purely national budgets; often, like space research or the *Mohole*, requiring immense vehicles and immense organization for their initiation; sometimes like CERN at Geneva, or *Dragon* at Winfrith Heath, involving international funds and wide implications in the field of foreign policy. Already a large number of international organizations, some bilateral, some regional, occasionally world-wide, some for research, others involving development, have sprung into being and require careful finance and clear thinking if they are to develop on the right lines. Clearly all these changes raise important implications for the relationship of universities to research, of universities to Government, and of universities to one another.

One such implication that is gradually becoming clear is that in certain branches of science it is impossible for every university to have equal treatment from the Government in all spheres. Ten linear accelerators each costing £1,000,000 will not make up for the absence of one linear accelerator costing £10,000,000—if one is needed; and it is quite clear that not every university can hope to have a £10-million accelerator. In Britain, at any rate for the time being, there can only be one Jodrell Bank, one *Nimrod*; there can only be a few gas-bubble chambers, and only a few research reactors. Where are these to be placed ? Who is to run them ? Who is to arrange their research programmes ?

When a number of such various projects are proposed by scientific enthusiasts, How are we to judge which to accept, particularly where these belong to different fields ? How are we to correlate the work of the National Institute for Research in Nuclear Science with the applications to the Department of Scientific and Industrial Research in the field of nuclear and high-energy physics—or with the budget of CERN in which we have only a minority vote ? How are the differing projects for radio astronomy to rank between one another or with the applications for big machines in other fields? How is either to rank with space research—another subject in which other countries are involved ? Can individual universities form partnerships or consortia ? Or should they all be provided for through a national extramural institution like the National Institute for Research in Nuclear Science ? If the latter, where is the facility to be placed—inconveniently for all universities, or conveniently for only one or two ? If a facility is given to one university, should any—and if so what—conditions be exacted for the benefit of the others ? If a facility depends on a particular man, what happens if he dies or resigns to move elsewhere ?

All these questions have actually arisen in a concrete form since I took office. Some I have had to decide. Some have been decided, with my approval, by the Research Councils. We are getting a certain amount of case-law and empirical wisdom about all this. But have we got it right ? This is something we shall have to discuss.

But it is not only a question of big expensive machines that can be located in or near only some of the universities. Somewhat similar problems arise out of the increasing diversification of subject-matter. How far is it necessary or desirable, for example, to preserve the existing situation in which the scope for postgraduate work by students of a given institution is often limited by the extent of the facilities—either natural or artificial—which that institution happens by tradition or by accident to have in its possession or in its close neighbourhood ? Clearly, university statutes were—or should be—made for the needs of learning; and not the needs of learning for the requirements of university statutes. Should university research still be limited in range by the migratory habit of medieval monks ? Should the availability of freshwater biology as a subject for research in Cambridge or Leeds be dependent on the contents of the Cam, or of the local Yorkshire factory effluent ? Should the availability of the Ph.D. to the staff of a Government research station depend on the place where each received his first degree ?

All these questions need public discussion. Government may have views; but in many cases it will be the vice-chancellors, the courts and senates, the faculties and the colleges, which supply the answers.

What is to be the relationship between courses of study and research in the universities and the known requirements of industry ? Distinguished academics often write to *The Times* expressing disquiet at the tendency of industry to demand courses from universities in fields which are remote from traditional fields and are of deliberate relevance to practical life—for example, management studies. Similar questions are asked in relation to industrial research and in some of the applied social sciences. Is industrial money corrupting, as the author of one letter appeared to think ? If so, ought we not to think the same of Government money ? With due respect to the University Grants Committee, and to the Research Councils, the Government is not fundamentally so disinterested as it pretends. Nor perhaps are even academics quite so pure. Nearly three-quarters of Government money going into scientific research goes on the defence budget. More of this than many people think is spent in the universities—and none of it could be spent at all without research workers, such as those who are trained in the Imperial College of Science and Technology.

My own view is that in Great Britain we should welcome and encourage industrial money, if only as a

desirable and necessary counterbalance to Government money. At least it is not motivated by war or the fear of it. Moreover, there is no academic doctrine more powerful than the motto of the Royal Society: "*Nullius in Verba*". When I am asked, as I sometimes am, whether it is not degrading that people should be asking for private donations towards cancer research, because the Government ought to bear the cost, I reply that I would not sleep easy in my bed if I thought that either I or the Medical Research Council were the only source of wisdom to decide which men and what ideas were worthy of support. The Americans may go a great deal too far academically in their dependence on private munificence; educationally they suffer enormously from the fact that their schools and universities are in no sense a Federal Government concern. But I think we may go too far the other way. From my point of view the degree courses available in British universities are too narrow in scope, and some of them are orientated too academically. I believe the same to be true to some extent of research work.

There is another important aspect to this. One of the most important subjects with which I am called on to deal is the relative failure of British industry to make use of science and the scientist. I will not bore you with figures; they are easily available. But, so far as I am concerned, the broad truth is that, outside a few main industries, far too few scientists are employed, and if more were employed some directors might not—in their present frame of mind—know what use to make of them. Not unnaturally, members of Parliament and others ask me what can be done to improve the situation. Whatever the immediate answer, I am quite certain that the only radical cure lies in the universities, in a closer contact with industry, both education-wise and research-wise. Contact between intelligent and right-minded people is not corrupting; almost invariably it is stimulating; and in my view at any rate academics have almost as much to learn from contact with industry as industry has to learn from the academics. Certainly, contact is the only way in which either will learn anything from the other. There is a great contrast between the extent of mutual regard and contact between academics and industrialists in Germany, which I have recently visited, and Britain. In my view, neither gains here by the degree of apartheid it practices: and, incidentally, if that apartheid were broken down, both in teaching and research, my own opinion is that the human sciences, which are excessively neglected in Britain, would also come into their own—both in the field of postgraduate research and in the field of new schools and faculties.

I realize that in making these remarks in the Imperial College I am rather preaching to the converted. The College's annual reports provide plenty of evidence of strong ties with industry, and of wise generosity by industry in financing work here on a variety of research projects; and there are also such things as the vacation training schemes by which students can gain valuable industrial experience.

But is this enough? Certainly in Germany you get co-operation between universities and industry to a much greater extent. To take only two examples: in Germany there are far fewer obstacles than exist in Britain to the combining of teaching with management or research in industry; and indeed, you get industrial concerns operating research institutes inside technological universities. I know, of course, that much can be said in support of the British attitude, the ideological division between teaching and production; but need we take it quite as far as we do? I shall not be so rash as to attempt an answer; but I feel it my duty to pose the question. When we see the close contact, amounting almost to organic unity, which exists between industry and universities on the Continent, and when we see some of the results in terms of design, production, and sales on one hand, and vigorous high-grade academic development on the other, we must surely ask ourselves whether the system adopted on the Continent does not possess certain competitive advantages which Britain lacks. I have spoken of the apartheid which seems to exist in Britain between universities and large sections of industry; may this not be due largely to the mere accident that many of our industries grew up outside the ambit of scientific and technological studies, and should we not see whether ways cannot now be found of bringing them together?

There can be no easy or single way of doing this. But one important need is the creation of the kind of climate of opinion in which industry and the universities turn towards each other quite naturally, and cross the gulf which has too often divided them hitherto.

Every one who at some stage or other in his career goes into industry, whether in industrial research or in production or general management, and every one who goes into Government scientific establishments or public administration, will not only be helping to bridge the gulf; he will also be able to spread among others the habit and the desire of making and maintaining the closest contacts with university teaching and university research. Similarly, those who remain within the university cannot unreasonably be asked to remember always the valuable help that those in the universities and those in industry can give to each other.

I must stress that it is not just a matter of doing well the research that comes to be tackled, or making use of the results of research when it is done; it is a question of research-mindedness, at all points: and here we come back to the very nature of the actual courses which the universities provide. Do they impart, along with knowledge, and skill in using knowledge, an adequate appreciation of the role of research, of the techniques of doing it, and of the importance of a readiness and a right way to apply its results? I ask this not only as regards postgraduate courses, where one ought to be able to hope confidently for an affirmative answer, but even more importantly as respects first-degree courses. Have the men who go out into industry straight after taking their first degrees—who after all comprise the main army of scientists and technologists—have they acquired, during their undergraduate training, a sufficient understanding—I will not say of research and of development—but even of design? Are they carrying a lighted flame—a torch with a battery—or just a reflector?

I do not need to labour the point: and let me make clear that in directing attention, as one particular topic that I feel needs special notice, to this question of contact in research between science and industry, I must in no way be taken as ignoring the importance of the more pure, more cloistered, more fundamental research that must also go on continuously if the well-springs of our science and technology are not to dry up. These are fundamental to the whole conception of scholarship—whether in the arts, or the natural sciences. In the long run it will be found

that the whole future of our civilization depends on the insights—I cannot refrain from calling them the artistic and creative imaginations—of a relatively small handful of men of genius, the true frontiersmen of knowledge.

I have posed a number of questions—and attempted few answers. Even some of the questions may be wrongly based—or wrongly put. But I hope at least that they will be food for thought—and I hope also that the course of development in our universities and colleges of advanced technology during the coming years will be such that the answers to these questions become increasingly reassuring.

I find myself at the end attempting to formulate a few general truths which seem to me to emerge from this discussion and from the wider experience which I have gained in the past four years.

If the general rule must be that research and university teaching cannot be divorced, the wider development of the subject implies inevitably closer contact between universities and Government research installations of one sort and another, between these and industry, between industries and universities, between universities and one another, between universities and places of research outside the general pattern which cannot conveniently be placed inside teaching institutions, between the scientific body within one national group and others of the same group—even between scientists of opposing groups of nations. These are not really rival conceptions for the organization of research; their rules are complementary rather than exclusive, and they are in truth part of a single complex, of a constantly developing conception of a scientific life gradually transforming the body of human society as we know it.

But, at the end of the day, if I am pressed with the familiar question of the egg and the chicken, if I am asked to define the point at which new growth is to be inserted into the scientific life of which I speak, I look, on one side, to the universities to provide the new ideas; but I accept the responsibility of Government to supply the initiative and the drive to convert these new ideas into actuality. The more I think of the problem confronting me as Minister for Science, the more I am convinced that the clue to the enigma lies in the universities and the colleges of technology; and where better to seek the answer to the riddle than at the Imperial College, which is in a sense both, and at a commemoration festival—an occasion when many are gathered together from both inside and outside the academic circle, many who are, many who have been, and many who will become leaders of thought in State, industry and learning.

The founders of the Imperial College, of course, visualized it as a centre of learning for a more or less centralized empire. Already that conception has given rise to that of a commonwealth of free and independent nations. But, speaking for myself, I see the centres of learning as something more than this. These are the true centres of culture in a nation. By improving these we take the shortest—indeed the only practical—course towards raising the standard of knowledge and civilization of the world.

MEDICAL RESEARCH AND THE NATIONAL INSTITUTES OF HEALTH, BETHESDA, MARYLAND*

By Dr. CARL R. BREWER
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THE National Institutes of Health, which began in 1887 as a one-room laboratory on Staten Island, New York, to-day comprised forty-two buildings occupying ninety acres of land in Bethesda, Maryland, north-west of Washington, D.C.

To understand the role of the National Institutes in health research, it is necessary to understand that the United States is one of the most health-conscious countries in the world; and that the American people have repeatedly expressed, through their representatives in the Congress, their fervent desire to wipe out disease and the crippling effects of disease and to help themselves and other nations to a new level of healthful well-being, and to longer and more productive lives.

That such goals always have been an integral part of the American philosophy is illustrated by the fact that the U.S. Public Health Service was established in 1798, that is, 163 years ago. That such goals run as a theme through all Departments of the U.S. Federal Government to-day is illustrated by the fact that several of these major Departments themselves also support biomedical research, in addition to the work done at the National Institutes of Health as a part of the Public Health Service and the Department of Health, Education, and Welfare.

The object is to give man a better life through research in medicine, by which is meant the medical sciences, the many portions of the biological sciences related to medicine, and those portions of the physical sciences related to medicine.

I will not go into the statistics related to the monetary size of these efforts. Figures on the numbers of dollars lack meaning in themselves. The dollars are simply the means to the ends of action and results in research—and action and results are what we are after. To help illustrate the point that the American people whole-heartedly are supporting the drive for better health, the percentage growth in the past twenty years is worth mentioning.

Since about 1940, total expenditures for medical research in the United States (that is, including the moneys of private foundations as well as the Federal Government) have increased more than 1,500 times. To-day, the Federal Government is supporting roughly 55 per cent of all medical research in the country, and the National Institutes of Health are responsible for about 75 per cent of the Federal Government expenditures.

Thus, the National Institutes of Health form the largest biomedical research institution in the United States, and probably the largest in the world. There are about 2,000 research scientists and approximately 6,000 administrators, laboratory technicians and other employees working at the various departments

* Substance of an address given before the International Symposium on Microchemical Techniques, at the Pennsylvania State University, University Park, Pennsylvania, on August 16.

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in Bethesda, Maryland. The total programmes of the Institutes are divided between the 'intramural' activities carried out at Bethesda and the 'extramural' activities under which the organization provides grants-in-aid support for biomedical research in the nation's schools of medicine, dentistry, public health, osteopathy, nursing and others; universities; and other private research institutions.

During the Fiscal Year 1961 (which ended June 30, 1961) the intramural programmes totalled approximately 85 million dollars.

Principal among the numerous buildings devoted to the intramural programmes is the Clinical Center, a 516-bed research hospital with 1,100 laboratory units and 1,260,400 sq. ft. of space. It employs more than 1,500 persons.

During the same year, the extramural programmes totalled approximately 475 million dollars (the latter having grown from 850,000 dollars in 1946). In this connexion, 13,500 research grants, 3,618 training grants and 4,205 fellowships in the United States and abroad were awarded.

Perhaps it seems an over-simplification, but it is accurate, to say that the National Institutes of Health are supporting and/or carrying out research in every biomedical science and nearly every disease known to man. At one extreme, they are supporting work on the very origins of life—how the amino-acids came together to form a primitive proteinoid, and developmental biology, embryology, genetics, and diseases of childhood. At the other extreme, the biological processes of ageing and the rehabilitation and home-environmental problems of older people are being examined. Literally, we are concerned with life from before conception to death, and all the stresses which assail man in his existence —organic disease, and psychological and environmental stresses.

Until 30–40 years ago the major causes of serious illness and death were the infectious diseases. These diseases received most of the attention of medical research because they were the major killers.

Then penicillin became available, followed by many other antibiotics; and while these certainly did not end the problems of infectious diseases they drastically changed the overall picture of medical research.

We cannot claim final victory over pathogenic micro-organisms because, obviously, they can mutate (and there exists, for example, penicillin-resistant *Staphylococcus*); thus, we are left with unsolved problems.

On the other hand, it is the chronic diseases, such as heart disease, cancer and others, which to-day have become the major killers. In the United States alone, different forms of cancer kill about 260,000 persons every year, and heart diseases account for nearly 900,000 deaths every year. So it is these diseases which are now attracting major attention, along with neurological disorders, arthritis and the entire spectrum of metabolic diseases, mental health, allergy, and dental disorders; and there we have the titles of the seven Institutes at Bethesda: Allergy and Infectious Diseases, Arthritis and Metabolic Diseases, Cancer, Dental Research, Heart, Mental Health, and Neurological Diseases and Blindness.

In terms of scope, the National Institutes have recognized the necessity of becoming concerned with the entire scheme of man's existence—the whole organism of man in relation to disease and his total environment, including both the psychological and physical.

As one example of the scope of research, the Institutes are providing new and increased opportunities for such para-medical scientists as anthropologists, biometricians and epidemiologists to clarify the relationships between cultural stresses and diseases, for example, as in the relationship between the high intake of fat in certain cultures and the incidence of atherosclerosis.

If, for another example, we consider the field of psychiatry, we find that it, too, is expanding beyond the limits of the office couch into environmental studies, on one hand, and yet also much deeper into the part that biochemistry may play in the origins of, as well as therapy for, mental and/or emotional disorders.

As to the depth of our research penetrations, I would like to quote Dr. James A. Shannon, director of the National Institutes of Health[1]: "Although until recently we were limited in our examination of the economy of the body as a whole—its net energy balance, the net exchange of foodstuffs, and the endocrine factors that were effective in producing changes in these—we are now able to isolate for study important specific systems within cells and to define with precision many of the discrete steps which characterize their activity. We can describe the components of these systems, quantitate the kinetics of the interactions involved, study the effect of superimposed variables upon these reactions, the products of which may be retained or released. By other techniques we can describe the importance of many of these systems to the cell, to the organ, to the organ systems and, in fact, to the body as a whole".

The pattern of much of the biomedical research in the world to-day is the pursuit of a much larger, broader, deeper, more integrated body of knowledge about basic human biology. The National Institutes have accepted this charge, and the acceptance of this new challenge has found wide expression in all the Institutes' programmes, particularly that of the Division of General Medical Sciences.

In effect, the Division of General Medical Sciences is the eighth Institute at the National Institutes of Health, because it functions as an Institute in all respects except that there is no intramural programme. The programmes are devoted entirely to grants to the medical schools, universities, research hospitals and other private research institutions. In the research training programme, which also is oriented toward the basic biomedical sciences, funds are provided to the medical schools and other institutions to aid in the training of new investigators. In the research fellowship programme, awards are made to individuals, at the predoctoral and postdoctoral levels, to aid the general research training development of scientists.

Until recently, nearly all the Division's research grants have been on an individual project basis, and the grants of this type in the Division of General Medical Sciences alone total approximately 2,000. One modification of this procedure came in the establishment of the General Clinical Research Center Program which provides funds to medical schools and research hospitals. The purpose of these grants is to broaden and intensify clinical research, particularly in the sense of achieving careful quantitative measurements of disease. The funds go for the establishment of discrete facilities or centres for the location of beds and laboratories. A variety of different research projects can be carried on in these centres. Another modification of the individual

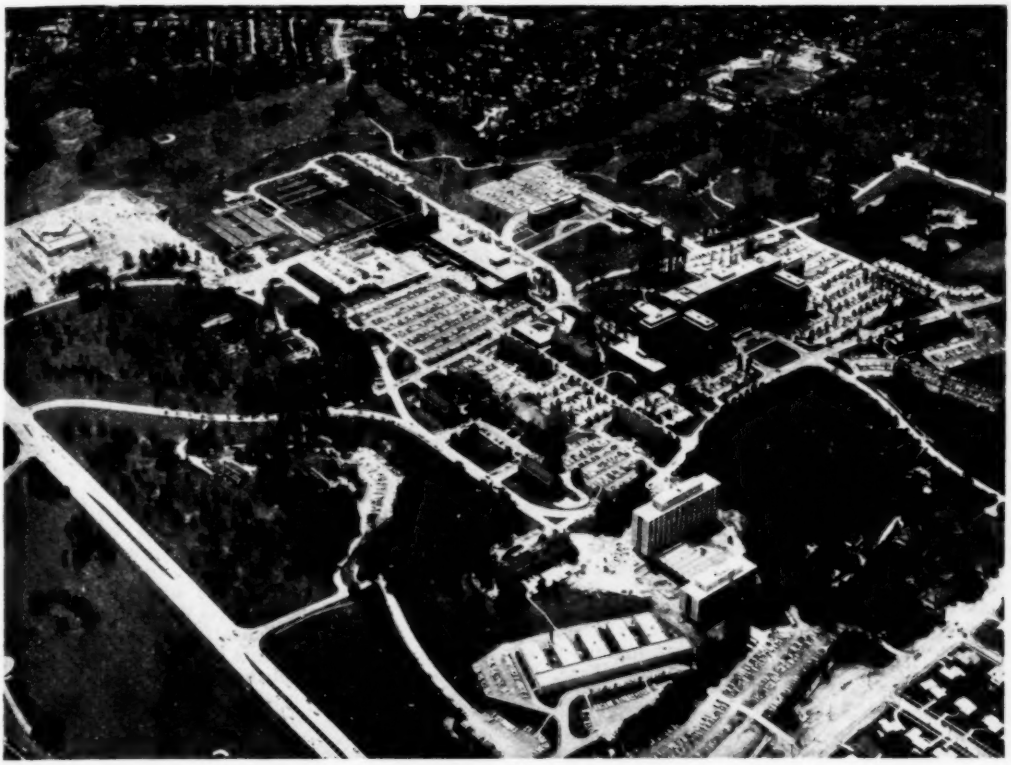

Fig. 1. The National Institutes of Health, Bethesda, Maryland, U.S.A.

project procedure is the new General Research Support Grants Program, which was recently initiated. This will provide the schools of medicine, public health, dentistry and osteopathy and other institutions with funds which these institutions may then use for the support of their research programmes. The feature which principally distinguishes this programme from most other National Institutes of Health and Public Health Service programmes is the even greater freedom given the institution in the use of these funds.

The establishment of the Division of General Medical Sciences just three years ago was an expression of the broader and deeper research approach of the National Institutes of Health. The research programmes of the Institutes have always involved basic research; but for the most part these programmes have been oriented to specific diseases. In the mid-1950's, there was recognized a need for more basic research, and basic research training, which was not disease-oriented. The National Institutes began making a number of grants for such purposes, and by 1958 it became apparent that the demand was such that a unit should be established especially for the administration and management of these grants. The reaction of the biomedical-scientific community to this development was such that expenditures for the Division's programmes have more than tripled since it was organized. During the past year, these programmes totalled nearly 85 million dollars. Further recognition of the importance of these programmes has come in a recent proposal by President Kennedy to the Congress that this Division be established as the National Institute of General Medical Sciences.

While the Division's activities are generally not oriented to specific diseases, their justification is the urgent need for basic biological knowledge essential for progress in the conquest of human diseases.

A simple example—but not a simple problem—pertains to research in the biological process of ageing and, more specifically, to recognition of the distinctions between the physiological ageing process and the pathological disease process.

Molecular biology is a field in which the Institutes are very active. One is sure that work in this area eventually will provide much additional information on such problems as rheumatic syndromes, infertility, tuberculosis, virus infections, cancer, hypertension, schizophrenia and alcoholism, because all these conditions involve disordered chemical processes of cellular metabolism.

In recent years, of course, modern biochemistry has come into its own, with its progress and expansion being such that it has fathered a number of subdisciplines and has become integrated into nearly all phases of medical research.

In the field of developmental biology, the Institutes are seeking to be as broad and deep as in biochemistry. Research is being supported in all phases and aspects of structure and function related to genetics and reproduction. These would include the germ cells and fertilization, the placenta, the fœtal fluids, the embryo and fœtus, teratology, parturition and lactation, and special problems of gestation.

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The field of genetics, of course, continues to grow at a tremendous rate, but we do not yet know its full significance in human biology and in disease. Dr. Jack Davies, of Washington University, St. Louis, has said: "How the genetic and environmental factors act and interact during development (of the fertilized egg) is perhaps the fundamental problem of biology"[2]. The implications with regard to congenital malformations and other hereditary diseases are, of course, obvious.

The work on the deoxyribonucleic and ribonucleic acids is beginning to provide a new concept of man and of disease. Among the great amounts of research that the Institutes are supporting in this field is that by some Israeli scientists on the role of the ribonucleoprotein complex of the cell in the synthesis of antibodies.

Modern geneticists are beginning to predict that man some day may be able to control his own biological destiny by influencing the genetic factors. This is one of the reasons for emphasis on medical and human genetics, cytogenetics, viral and bacterial genetics, biochemical genetics and genetic ultra-structure.

There are many other basic fields in which the National Institutes are also active. Examples are: public health and nursing; biomedical instrumentation; research surgery; anæsthesiology; bio-organic and biopolymer chemistry; biomathematics; and biophysics.

As the American interest in biomedical research and improved health is integral to all elements of the U.S. Government, so also is it an interest to be shared with the other countries of the world, for mutual benefit.

Such an effort has two goals: the first is the interchange of newly developed fundamental knowledge among the scientists of the world; and the second is the equally substantive advantage in biomedical research of learning more about the incidence and variable characteristics of specific diseases and also general biological phenomena in different parts of the world, as related to variations in climate, altitude, food, culture and other factors.

Just a year ago, the President of the United States signed the International Health Research Act of 1960. In general, the Act provides for support of research activities in foreign countries, research training and fellowships, the making of grants and loans of equipment, the support of international health research meetings, and the exchange of research scientists.

For the Fiscal Year 1961, just passed, a sum of 5 million dollars was designated for the development of activities under the Surgeon General's authorities provided by this Act. Approximately a half this amount was allocated for the development of a series of international centres for medical research and training, based in United States universities with overseas extensions in the form of research laboratory training facilities.

Each of the centres consists of, first, a professional, university-based organizational entity which provides a stable, continuing framework in which programmes of medical research, research planning and research training may be conducted in the United States, and which is associated with the second part, a research and training establishment abroad where these activities may be pursued under environmental, ethnic, and medical conditions which do not prevail in the United States.

The remaining 2·6 million dollars are to be utilized by the several Institutes and the Division of General Medical Sciences for the support of research projects involving foreign investigators and institutions, and directed toward research and research training objectives of key significance to these projects.

The National Institutes of Health recently established an Office of International Research, within the office of the Director of the Institutes. This new Office has the responsibility of advising the Director and the Office of the Surgeon General on the international aspects of medical research and research training. It also assists the Institutes and the Division of General Medical Sciences in the further development of international projects, and provides a mechanism by which the National Institutes of Health can work with international organizations, foreign institutions and scientists on a planned, predictable, long-range basis.

In years past, there has been talk about the need for an international language. We already have an 'international language' in the field of biomedical research. It is a subject which transcends geographical boundaries and defies language barriers. It is the goal of the National Institutes of Health and the whole American Government to improve and expand this 'language' to bring all the countries of the world closer together in the common cause of good health for all men.

[1] Shannon, J. A., *Philadelphia Med.*, **58** 699 (1960).
[2] Davies, Jack, *Survey of Research in Gestation and the Developmental Sciences* (Williams and Wilkins, Baltimore, 1960).

RUTHERFORD JUBILEE INTERNATIONAL CONFERENCE ON NUCLEAR PHYSICS

THE fiftieth anniversary of the publication of Rutherford's 1911 paper announcing the discovery of the atomic nucleus was celebrated by an international conference during September 4–8 at Manchester on what is nowadays called 'low-energy' nuclear physics. The conference was attended by more than four hundred people; its wide support will undoubtedly make it the major international meeting in its field in 1961.

As is usual with these almost annual events, progress during the past year was summarized; but on this occasion half a day was set aside from the discussion of present problems for a commemorative session on Rutherford's discovery. There were talks on their reminiscences by Sir Ernest Marsden, Sir Charles Darwin, Prof. E. N. da C. Andrade, and Prof. Niels Bohr, all of whom had worked with Rutherford at Manchester. Sir James Chadwick was present on the platform but did not speak. In these talks there came to life a period which to many of those present had been a legend they had read about only in text-books. Here was the tale of

Marsden whom Rutherford told to look for the reflexion of α-particles from solids, something which neither Rutherford nor Marsden expected to happen; but Marsden knew that if the effect existed and he missed it, that would be the end of him. Then there was Darwin's story of collaboration with Moseley, whose methods of non-stop work made him not only an expert on X-rays but also on where to get a meal in Manchester at three o'clock in the morning. Niels Bohr closed the session with a few brief remarks in which he laid special stress on the central importance of Rutherford's discovery in providing a testing ground for the theorists during the development of the quantum theory beyond the point to which Planck and Einstein had taken it.

The remainder of the conference was conducted in an atmosphere moulded by the portrait of Rutherford which looked down on the participants over coffee, and the presence of an exhibition of much of his apparatus. The complete proceedings will be published soon, so that here there is no need to mention more than a few topics the selection of which from the wealth of material presented is to a large extent a matter of personal taste.

There was steady progress to report on several fronts. The question of the fundamental origin of the interaction between nucleons has become clearer in recent years with the accumulation of evidence that the component of longest range is what would be expected from the exchange of single π-mesons. Further evidence of this effect has now come from an extensive analysis of the scattering of nucleons by nucleons in states of high relative orbital angular momentum where the centrifugal barrier makes the effects of longest range predominate; as it should, the strength of the coupling between nucleons and mesons required turns out to be the same in neutron–proton and proton–proton scattering, and agrees with that needed to account for the scattering of π-mesons by nucleons. The dependence of the long-range interaction on the spins of the nucleons also agrees with the theory. A new development in the field of nucleon–nucleon interactions is a direct measurement of the strength of the interaction of two free neutrons by means of the reaction $D(n,p)2n$ at low energies which is strongly influenced by the interaction of the two outgoing neutrons; the first result is not far off the value to be expected from p–p scattering on the grounds of charge-symmetry. Another problem which is at last showing signs of being cleared up is the origin of the spin-orbit coupling between two nucleons which had been introduced phenomenologically to account for scattering at high energies; this is probably connected with the existence of a short-lived quasi-bound state of three π-mesons of angular momentum unity—the '3π-resonance'—the discovery of which was announced at the conference. The spin-orbit coupling would arise analogously to that which acts between two electrons due to the electromagnetic field.

Some fundamental points in connexion with the shell model are still being elucidated, in particular the origin of the strong spin-orbit coupling seen by each particle in a nucleus, and the existence and properties of the low-lying single particle states which are not normally involved in low-energy reactions. The origin of the spin-orbit coupling probably also lies in the newly discovered 3π-resonance, through a mechanism analogous to the production of the spin-orbit coupling in atoms. The low-lying single particle states are now beginning to show up in $(p,2p)$ experiments; the incident protons have an energy of about 150 MeV. and are able to knock a proton out of the target, the spectrum of the summed energies of the two emerging protons showing clearly defined peaks corresponding to the binding energy of the ejected proton. The measurements on isolated nuclei which were previously available have now been extended until the binding energy of the lowest-lying level—the 1s—has been traced for elements up to atomic number 20. The same experiments can also give the original momentum distribution of the struck nucleon from the angular correlation of the emerging protons.

There was much discussion of two aspects of nuclei which go qualitatively beyond what can be described by the simple shell model built up from the picture of individual nucleons moving in a static potential well. These were the structure of the nuclear surface, where there may be important clustering effects, and collective motions in which many particles partake coherently in such a way as to generate an oscillating or rotating potential well. On the structure of the nuclear surface, new evidence produced during the previous year supports the view that the surface is probably more 'lumpy' than a simple shell model would lead one to expect. This evidence comes partly from new estimates of the probabilities of α-particle emission in some heavy nuclei on the basis of shell model wave-functions which give values smaller by about a factor 10^2 than the experimental ones. There is also new information on the absorption of K^- mesons at the periphery of a nucleus from bound Bohr orbits, where the existence of correlations between the nucleons can be detected by the possibility of the production of very energetic hyperons in absorption mechanisms such as $K^- + 2$ nucleons → hyperon + nucleon, in addition to the less-energetic hyperons which are emitted in the process K^- + nucleon → π-meson + hyperon, which is the only one to occur for free nucleons. The situation is not clear because it appears that in the light nuclei, in contrast to the heavy ones, it is possible to account for the emission and absorption of compound particles with a simple shell model without recourse to any additional clustering.

The field of collective oscillations is still developing under the new impetus it received from the discovery of the importance of particle-hole pairs and of pairing correlations at the top of the Fermi sea. So far most of the emphasis has been on quadrupole and octupole shape oscillations, and on the giant dipole resonance in which the protons oscillate against the neutrons. The theory gives the frequencies of collective oscillations in terms of the energies of the single particle excitations which contribute, and the probabilities of occupation of the single particle-levels involved. Measurements of these properties by means of stripping reactions now exist in a limited number of nuclei, and the collective frequencies calculated from them are found to vary from nucleus to nucleus in agreement with the measured values. However, in the prediction of electromagnetic transition probabilities the theory is still only in semi-quantitative agreement with experiment.

A welcome contribution was a talk under the title of "Rutherford and Nuclear Cosmochronology", by W. A. Fowler, who discussed the present estimates of the ages of the Earth, the solar system and the Galaxy, making use of the known abundances of the

elements and of calculations of these abundances from the synthesis of the elements in stars and supernovæ. It turns out that where Rutherford in 1929 gave the age of the solar system as $3{\cdot}4 \times 10^9$ years, the best present estimate is still as close as $4{\cdot}5 \times 10^9$ years.

The success of the conference amply repaid the members of the organizing committee for their labours. If they have one regret, it is that the limited space available made it necessary to refuse a place to many whom they would have liked to have seen. If some active and distinguished research workers feel disappointed at our inability to invite them, may we ask them to bear in mind that the places which were due to them probably went to representatives of isolated institutes for whom these conferences are the only real contact with the main stream of research in nuclear physics.

A. Herzenberg

ENDOCRINOLOGY AND EVOLUTION

During the recent meeting at Norwich of the British Association for the Advancement of Science a symposium on "Endocrinology and Evolution" was held under the auspices of Section D (Zoology), with Prof. C. M. Yonge in the chair.

In the opening paper, Prof. E. J. W. Barrington pointed out that while far too little is known about the ways in which hormones exert their effects, it seems evident that there must be a closely adaptive relationship between the active hormonal molecules and their target cells. This raises the questions when, and in what circumstances, these relationships were first established, questions which are important because the answers to them can scarcely fail to enlarge our understanding of the primary functions of the hormones concerned. He developed this theme with particular reference to the thyroid gland, an organ which shows a remarkable uniformity of biochemical organization through the vertebrates, from the cyclostomes to the mammals. Its characteristic iodinated tyrosines and thyronines are known to be produced in the endostyle of the ammocœte larva of the lamprey, before this organ has been transformed at metamorphosis into the definitive thyroid gland. It would appear, therefore, that any search for clues to the mode of origin of the gland must take us outside the vertebrates altogether.

Here we cannot fail to be struck by the fact that iodine has long been known to be present, and often in great abundance, in many marine invertebrates. Our knowledge of this phenomenon has been greatly extended in recent years by the use of radioactive iodine, and by employing the techniques of autoradiography and paper chromatography. These have shown that the organically bound iodine of marine animals is not strictly of a thyroidal character, for instead of being bound within thyroglobulin molecules it is commonly associated with the scleroproteins of the skeletal tissues. These have been closely studied in the Anthozoa and sponges, and it has been found that their iodine content may be surprisingly high, as much as 10 per cent as compared with the 1 per cent of thyroglobulin. It seems likely that the amount of iodine taken up by the scleroprotein molecules depends on their tyrosine content, and that it is mainly bound as monoiodotyrosine and diiodotyrosine, although trace amounts of thyroxine and triiodothyronine have been reported present in the horny skeleton of gorgonids.

The organic binding of iodine in invertebrates thus appears to be a chance consequence of the molecular constitution of their skeletal tissues, and this raises the question whether there is any evolutionary relationship between it and the highly specialized iodination sequences of the thyroid gland. We cannot be sure of the answer to this; but consideration of the results of recent work on the protochordates, which are known to be closely related to the vertebrate line of ancestry, suggests some interesting reflexions. Autoradiography has demonstrated the occurrence of iodine binding in certain clearly defined cells of the endostyles of ascidians and amphioxus, and chromatography has shown that iodinated tyrosines and thyronines are present in these animals. There is some evidence that these substances may be associated with the specialized outer layer of the tunic of ascidians, as well as with the endostyle, so that these particular animals may eventually be found to show random iodination side by side with the endostylar process which foreshadows the eventual emergence of a true thyroid gland.

It is attractive to speculate that iodinated products arising thus by chance in early chordates might have become metabolically available for the animals, by ingestion or by transport in the blood stream, and that increasing dependence on these would have led to the evolution of a more efficient biosynthetic mechanism in the endostyle. At the present time this is no more than a thought to guide further investigation; but we certainly cannot dismiss the possibility that the thyroid hormones evolved as a result of animals incorporating into their biochemical organization substances which were initially presented to them as random biological products.

Any discussion of the evolution of hormones needs to take account of the fact that they do not act in isolation, but as components of highly integrated systems of mutually interrelated glands. Prof. J. M. Dodd was to have discussed this aspect with particular reference to the work of himself and his colleagues on the relationship between the pituitary and the thyroid; but he was unable to attend, so his place was taken by Dr. K. M. Ferguson, who began by remarking that although the controlling influence of the pituitary over the thyroid, mediated by its thyroid-stimulating hormone, is well known in mammals and amphibians, it is not always so easy to demonstrate it in the other vertebrate groups. Nevertheless, there is ample evidence of a qualitative nature to demonstrate that this so-called pituitary-thyroid axis is probably common to the entire vertebrate series. For example, although neither removal of the pituitary nor administration of mammalian thyroid-stimulating hormone produces significant histological changes in the thyroids of adult elasmobranchs, Dent and Dodd have shown that a distinct thyroid–pituitary interrelationship exists in the immature, newly hatched dogfish, *Scyliorhinus canicula*, and that its thyroid-stimulating hormone is probably located in the ventral lobe of the pituitary.

Quantitative evidence is scanty, but by using the mouse assay of McKenzie it has been possible to

demonstrate thyroid-stimulating activity in pituitary extracts from animals ranging over the entire vertebrate series, although at considerably lower concentrations than are found in mammals. Certain features of these results, however, present difficulties of interpretation. For example, a large part of the activity is heat-stable, while mammalian thyroid-stimulating hormone is markedly heat-labile. Moreover, measurable activity is obtained from the neural lobe, even in the mammal, although there is every reason for regarding thyroid-stimulating hormone as a product of the adenohypophysis. The significance of these facts is bound to remain obscure until we are better informed of the chemical nature of thyroid-stimulating hormone; but in the meantime it is necessary to remember that glandular extracts may contain a large number of contaminants, hormonal and otherwise, which are likely to interfere with responses, and which cannot be adequately controlled by injections of indifferent tissues such as brain or muscle. It is possible, too, that foreign pituitary material may set up interfering stress responses, while it is known that the relative thyroid-stimulating potency of extracts from different species varies according to the choice of the assay animal.

These considerations combine to make it impossible to decide whether the apparently low concentrations of the hormone in extracts of pituitaries of the lower vertebrates reflect quantitative or qualitative differences. It may be, however, that the thyroid-stimulating hormone molecule has been subjected to biochemical evolution, but has yet retained sufficient community of chemical structure throughout the vertebrates to allow pituitary extracts from a wide range of donors to stimulate the thyroids of a wide range of recipients.

Further aspects of endocrine evolution were brought to light in Dr. J. G. Phillips's discussion of the adrenal gland. There is much variation in the gross appearance of this organ, and in the degree of association of its two components, the chromaffin and the adrenocortical tissue, but these variations, characteristic of each of the main vertebrate groups, mask a remarkable constancy in the properties of its secretory cells. This is well illustrated by the steroid hormones of the adrenocortical tissue, which appear to be chemically identical throughout the vertebrate series, and which are involved in homeostatic mechanisms contributing in one way or another to ensure a constancy of the internal medium. Nevertheless, this fundamental uniformity has not prevented the establishment of a wide degree of functional adaptive radiation. In the sphere of water and salt metabolism, for example, these hormones influence tissues such as the nephron, the gills of fish, and the skin and bladder of frogs, all of which share a common capacity for the transcellular conduction of electrolytes and water, and which react to adrenocortical hormones in a manner determined by the nature of the environmental hazards to which the particular species is exposed. Thus, marine fish are faced with the problem of retaining water and excreting excess salts, while the converse situation confronts freshwater species, and these hormones, although not the only factors involved, contribute to the necessary physiological adaptations by their action on the kidneys and the gills. In sea-water they promote the excretion of excess electrolytes through the gills, and the maximal re-absorption of water in the kidneys, while in fresh water they promote the excretion of large volumes of dilute urine, accompanied by salt retention.

It is evident that one important factor in the evolution of endocrine systems is the possibility of change in the character of the target organs, and Dr. Phillips illustrated this by reference to recent work on the remarkable ability of marine birds to survive for long periods the ingestion of fluids which have an ionic concentration many times higher than that of their body fluids. This ability depends on the nasal glands, situated above the eyes. Following the ingestion of sea-water, these glands are activated, and, as a result of their remarkable concentrating ability, the bird excretes the excess salt through the nasal gland without commensurate loss of water. The action of the adrenocortical hormones is one of the factors involved in this response, and there is evidence that, with the hormones of the neural lobe of the pituitary, they arrest the excretion of the excess salt through the kidney; this is then followed by a shift to the physiologically more economical method of excretion through the nasal glands. There is good evidence that the latter are also dependent on the nervous system, but at present it is not possible to judge the relative importance of the two forms of control. It is clear, however, that the action of the adrenocortical hormones on the nasal glands is closely analogous with their action on the gills of marine fish, for in both cases they serve to promote the excretion from the body of excess salt without undue loss of water.

The final paper was given by Dr. D. B. Carlisle, who reviewed some problems of crustacean endocrinology, and this was followed by a lively discussion which ranged over such diverse problems as sex-reversal in molluscs, the function of indole derivatives in crustaceans, the influence of ciliary feeding in the evolution of the thyroid gland, and the possible role of adrenocortical tissue in the metamorphosis of lampreys. The session as a whole must have done much to reassure those who fear that endocrinology, with its para-medical background and its esoteric terminology, is too specialized for comprehension by the general biologist, and it amply demonstrated how widespread are the biological problems which are being illuminated by present developments in the comparative study of endocrine mechanisms.

E. J. W. Barrington

OBITUARIES

Prof. H. P. Robertson

Prof. H. P. Robertson, who contributed to the theories of relativity and cosmology, and was a member of many Government scientific boards in the United States, died on August 26 as a result of injuries sustained in a motor-car accident. His death takes from many people throughout the world a sensitive, gay and ever-helpful friend as well as an experienced and wise counsellor.

He was born in Hoquiam, Washington, on January 27, 1903, and received his bachelor's and master's degrees in 1922 and 1923, respectively, from the University of Washington, where he was introduced to the Einstein theory of relativity by E. T. Bell.

XUM

He obtained the Ph.D. degree from the California Institute of Technology in 1925 and then spent two years in Germany as a National Research Fellow at Göttingen and Munich. He joined the Mathematics Department of the California Institute of Technology as an assistant professor of mathematics for the period 1927–29.

During 1929–47 he was at Princeton University, occupying successively the posts of assistant professor, associate professor and professor of mathematical physics. In 1947 he returned to the California Institute of Technology as professor of mathematical physics, a post he held until his death.

Although Robertson devoted most of his scientific efforts to the general theory of relativity and to its application to cosmological problems, he was interested in the foundation of physical theories and the application of various branches of abstract mathematics to physical problems. His excellent translation of Herman Weyl's *The Theory of Groups and Quantum Mechanics*, which he completed in 1931, demonstrates his profound knowledge of the theory of groups, quantum mechanics and the relationship existing between these two subjects.

He was a master in applying the theory of groups of motion of Riemannian spaces to problems in relativity. His 1933 paper entitled "Relativistic Cosmology", which appeared in the *Reviews of Modern Physics*, illustrates his use of the technique. In this classic paper he summarizes his own basic work and that of others on the consequences of the symmetry assumptions made in relativistic cosmology and relates these to the astronomical observations. He afterwards studied the implications of the symmetry assumptions alone, divorcing these from the Einstein field equations. The latter work was stimulated by the lively controversy over kinematical relativity, in which he and E. A. Milne engaged, and appeared in three papers and in the *Astrophysical Journal* (1935, 1936) entitled "Kinematics and World Structure".

Robertson's contributions to relativity should not be measured only by his own papers. He engaged in extensive discussions with, and participated in the work of, others. His aid is acknowledged by many authors; in particular, he played an important part in the work of Einstein, Infeld and Hoffmann on the equations of motion of singularities in the gravitational fields and published his solution of the equations for two bodies with comparable masses obtained by these authors.

In 1939 Robertson responded to a call from his friend and mentor, R. C. Tolman, and began his work on scientific problems important to United States military agencies. He stopped his intensive work in relativity, which was just coming to fruition, and answered to the demands made on him with characteristic vigour. He quickly produced a scholarly review of work in terminal ballistics and made contributions to this field. He took an active part in organizing the group that became Division II of the National Defense Research Committee and in directing the early work of this group.

He served with the National Defense Research Committee from 1940 until 1943 and as scientific liaison officer, London Mission, Office of Scientific Research and Development, during 1943–46. From 1944 until 1947 he was an expert consultant to the Office of the Secretary of War. In 1945 he was chief of the Scientific Intelligence Advisory Section of Supreme Headquarters, Allied Expeditionary Force in France. For his war service he received the United States Medal of Merit.

In 1950 he was called back to Washington and served for two years as deputy director and research director of the Weapons Systems Evaluation Group of the Department of Defense until 1952. During 1954–56 he was the scientific adviser to General A. M. Gruenther, the then Supreme Allied Commander in Europe. For four years beginning in 1956 he was member at large and chairman of the Defense Science Board. He was also a member of the President's Scientific Advisory Committee.

In addition to belonging to a number of scientific societies, Robertson was a member of the U.S. National Academy of Sciences, of which he was foreign secretary from 1958 until his death.

Although Robertson never lost his interest in working in the theory of relativity and in teaching this subject, his many Washington duties to which he gave himself unstintingly made it impossible for him to do more than publish a few papers after the Second World War. In some of these he again reviewed the theoretical and observational state of the theory of cosmology. He was much interested in the possibilities of using satellites for experimental tests of theories of gravitation and took part in organizing, and was chairman of, a conference on this subject in July last at Stanford University.

This review of some of Prof. Robertson's achievements and activities must of necessity omit much that should be said about him. Suffice it to say that he made his mark in science, in service to his country, and in the hearts of the many people from all walks of life who were privileged to know him.

A. H. Taub

Mr. Lewis Eynon

The news of the death on October 18 at the home of his son at Stoke Bishop, Bristol, of Lewis Eynon will sadden his friends in many countries. The sugar industry has lost a most experienced analyst, who further had done so much to help the analytical profession. Eynon was born in 1878 at Stoke Newington and was educated at the City of London School. On leaving there he became a student at Finsbury Technical College during 1895–99 under Prof. Meldola. He was then appointed a chemist to the Beetroot Sugar Association. Another Finsbury student, J. H. Lane, was also there with him, and the two became partners in 1910 as consulting chemists. Having acquired the laboratories from the Sugar Association of London, as it had then become, and also the business of the analysis of its sugar samples, they had spare time which they used for research on sugar, chiefly on improvement of methods of sugar analysis. Their long search for a sensitive internal indicator for use with Fehling's solution for testing reducing sugars eventually led them to methylene blue. The result was the Land and Eynon method which has become well known throughout the sugar world. It has eventually been accepted as an official method by many countries and also by the International Commission.

Eynon obtained many qualifications and held many important offices among the various professional bodies to which he belonged. In 1900 he gained the associateship of the Royal Institute of Chemistry and was elected to the fellowship in 1903. A year later he graduated B.Sc. at the University of London with honours in chemistry. For many of the years between

1920 and 1949 he served on the Council of the Royal Institute of Chemistry, and during 1930 he was a vice-president. An early member of the Society of Public Analysts (later the Society for Analytical Chemistry) he served on the Council, was honorary secretary during 1936–47 and president during 1947–49. He attended the meeting of the eighth session of the International Commission for Uniform Methods of Sugar Analysis, held in 1932 at Amsterdam, and was elected honorary secretary, in which position he remained until the end of the ninth session in London in 1936. He was also chairman of the Publication Committee, responsible for the production of the *Proceedings* for the eighth, ninth, and tenth sessions. In 1932 he became honorary secretary of the newly formed British National Committee of the Commission, which position he relinquished in 1948 to become chairman. This post he held until 1954. The same year in Paris at the eleventh session of the Commission he was unanimously elected life honorary vice-president "in grateful recognition of his extensive and valuable services to the work of the Commission and for his distinguished contributions to the literature and practice of sugar analysis".

At the end of more than sixty years of a very busy life, he was still the same gentle-mannered man, a very kindly character, unassuming and loved by all who knew him; his many friends could count on the encouragement and help that was always forthcoming.

H. C. S. DE WHALLEY

NEWS and VIEWS

Nobel Prize for Physics:

Prof. Robert Hofstadter

PROF. ROBERT HOFSTADTER, who shares the Nobel Prize for Physics with Prof. R. L. Mössbauer, was born on February 5, 1915; he received the bachelor of science degree from the City College of New York in 1935, and his Ph.D. from Princeton in 1930. He then taught and carried out research at Princeton, Pennsylvania, and the City College of New York until the war years, during which he worked at the National Bureau of Standards and the Norden Laboratory Corporation. For four years after the War he was assistant professor at Princeton, but in 1950 he went to Stanford as associate professor, becoming professor in 1954, and eventually head of the department. Prof. Hofstadter is best known for his use of high-energy (roughly 1 BeV.) electron beams to probe the structure of nucleons. A knowledge of the form of the meson clouds surrounding the proton and neutron has been at the foundation of important recent developments in quantum field theory. It is not possible to give an adequate idea of this work in a short space; but the success of his work is perhaps best illustrated by the discussion it provoked in the United States of the feasibility of constructing an electron accelerator of still higher energy.

Prof. R. L. Mössbauer

THE early recognition of the importance of Prof. R. L. Mössbauer's work by a share of the Nobel Prize for Physics will give great satisfaction to all physicists. The recognition might have been even earlier if Prof. Mössbauer's work, carried out at the Max Planck-Institut at Heidelberg in 1957, had not passed strangely unnoticed for nearly two years. The discovery of what is now called the 'Mössbauer effect' is concerned with the spectrum of the γ-rays which are emitted by certain excited nuclei. It has been known for many years that the nuclear levels in many cases are extremely sharp, but considering the problems of nuclear recoil and lattice vibrations which introduce Doppler shifts, physicists had resigned themselves to the conclusion that the very narrow γ-ray lines which exist in principle would remain for ever inaccessible. Mössbauer's achievement lies in recognizing that in certain specific cases, appreciable fractions of the γ-rays may be emitted undisturbed by recoil or lattice vibrations. The imaginative achievement is the more remarkable when one considers that the theory underlying the effect has been known for twenty years, but the relevant inferences had not been drawn. The first spate of new results obtained by making use of the Mössbauer effect in experiments to test the predictions of relativity theory, to investigate the properties of the solid state, the nature of magnetism and the properties of some nuclear excited states has now subsided, but there can be no doubt that the application of the discovery will continue to be a subtle tool in all branches of science.

Nobel Prize for Chemistry :

Prof. M. Calvin, For.Mem.R.S.

PROF. M. CALVIN, who has been awarded the Nobel Prize for Chemistry for 1961, took his doctorate at the University of Minnesota and afterwards spent two years at the University of Manchester with the aid of a Rockefeller Grant. In 1937 Prof. Calvin joined the staff of the University of California. Discovery of the long-lived isotope carbon-14 during the War (prior to which only the short-life isotope carbon-11 had been available) provided an opportunity for a comprehensive study of the intermediates of photosynthesis which was immediately realized by Prof. Calvin. Success came when the isotope technique was combined with the then recently discovered paper chromatographic method of analysis. In work with A. A. Benson and later others, the first product of the photosynthetic fixation of carbon dioxide was shown to be phosphoglyceric acid and for the first time the importance of the pentose and heptulose phosphates in photosynthesis was realized. Calvin postulated a sequence of reactions constituting the 'photosynthetic cycle' in which these compounds formed a synthetic cycle for the incorporation of carbon dioxide. About the same time essentially the same reactions were shown to play an important part in the respiratory process (the pentose phosphate shunt) not only of plants but also of animals. The interests of Prof. Calvin's group have now moved towards the investigation of the basic mechanism by which light energy is converted into chemical energy in the chloroplast of the green plant. Attempts have been made to devise model systems in which light energy can be converted to chemical energy with high efficiency, thus necessitating an extension of the earlier studies of the photochemistry of dyes. Prof. Calvin was elected a foreign member of the Royal Society in 1959.

XUM

Nobel Prize for Physiology : Dr. Georg von Békésy

The award to Dr. Georg von Békésy of the 1961 Nobel Prize for Physiology gives recognition to a remarkable achievement in the field of experimental biophysics. Dr. Békésy has had an unusual career. Born in 1899 in Budapest and educated at the Universities of Bonn and Budapest, he has, since 1949, been senior research fellow in psychophysics at Harvard. He has displayed outstanding skill as an experimenter, devising at all stages of his work new technical equipment, mechanical, optical and electrical, of great ingenuity. His first remarkable contribution was a penetrating analysis of the vibrational responses to pure tones of the basilar membrane of the human cochlea. A later outstanding achievement was his use of vibrating electrodes to explore and reconstruct the patterns of amplitude and direction of vibration induced in individual cell elements within the cochlea in response to pure tones of varying frequency and intensity. His papers, written in clear, concise and graphic language, have exercised a profound effect on our concepts of the peripheral mechanism of hearing. An edited selection of his earlier German papers has recently been translated into English by Prof. E. G. Wever, one of his American colleagues, and republished together with others in book form, *Experiments in Hearing*. This is a substantial volume of 750 pages and incorporates a representative bibliography of the author's papers. In 1961 Dr. von Békésy was awarded the Gold Medal of the Acoustical Society of America.

The Education Bill in Great Britain

The Education Bill, which received its second reading in the House of Commons on November 13, has two purposes. The first is to provide statutory authority for the reforms in the system of grants to students which were announced following the report of the Anderson Committee; the second is to reduce to two the number of school-leaving dates in the year, as recommended by the Central Advisory Council for England and Wales in the Crowther Report. In moving the second reading of the Bill, the Minister of Education, Sir David Eccles, said that the local authorities, with which he had fully discussed the provisions of the Bill, readily accepted that the time had come to make the awards automatic when the student had both the qualifications and a place at a university, and Clause 1 laid this duty on the authorities as from September 1962, and gave the Minister power to define the extent of the duty. Sir David said that he had accepted the Anderson Committee's recommendation that the qualifications for an award should be two A-level passes in the General Certificate of Education, but it is necessary to provide for further qualifications which students may gain as they advance in technical colleges. Clause 2 ensured that local authorities had full discretion to make awards for further education courses below the standard comparable with first-degree courses.

The second fundamental principle of the new system is uniformity of treatment. Sir David said that local education authorities now generally accept for the student's own maintenance during term the standard figures reviewed at intervals by their representatives and the Ministry. In future there would be nationally prescribed rates and conditions of grant binding on all authorities for all items of a student's grant which could be dealt with in this way. It was proposed to retain the means test in a relaxed way which would relieve about 10,000 more families from all contributions and those in the middle range of incomes would pay substantially less. Grants for students in teacher-training colleges would be calculated in the same way as for university students, and those for students in technical colleges taking full-time courses comparable with degree courses would be similarly calculated. The standard vacation grant had been revised and now applies throughout the income range of parents, while conditions for dependants' grants have been revised and broadened. Students may keep up to £100 of private income, including income from scholarships and prizes, without deduction from their grant, and the Minister said he had appointed a Standing Advisory Committee with Sir Francis Hill as chairman to advise on matters relating to the size of the grant and the definition of 'comparable courses'. The Committee had been asked to recommend revised rates of grant early in the New Year.

Sir David said that under our present policies, the cost of education in Britain is rising at about 5 per cent a year, and awards to students now cost £35 million a year. What is proposed under the Bill would add a further £10 million. To abolish the means test altogether would add another £10 million, and Sir David said that if he and the Secretary of State for Scotland were allowed to spend a second £10 million, they thought they could spend it to better advantage in other parts of the service. Under Clause 3 of the Bill, State Scholarships would disappear, but the Minister intends to retain the scheme for mature State scholars, and his powers to operate the State studentship scheme of awards for postgraduate students in arts subjects are also continued. As regards school leaving, under the Bill a child who reaches fifteen in the months September–January must stay at school until the end of the Easter term; if he reaches fifteen after the end of January, he must stay to the end of the summer term. The Bill also applies to Scotland the automatic awards, uniformity of treatment, revised income scale and other improvements, but the Scottish Education Department will itself make the awards to students in universities and similar institutions of higher education.

Scientists and Engineers in the U.S. Federal Government

A report, *Scientists and Engineers in the Federal Government, October* 1958 (NSF 61–43. Pp. vi+44. (Washington, D.C.: Government Printing Office, 1961.) 35 cents), issued by the National Science Foundation, also includes some data on trends in Federal employment of scientists and engineers since the previous report (covering the year 1954). In 1958 the Federal Government employed about 8 per cent of all full-time 'white-collar' workers, an increase of 20 per cent on 1954. Of these 121,000, 55,000 were engineers, 21,000 were biological scientists and 18,000 physical scientists. The Department of Defense was the largest employer, and some 75 per cent of the total were employed outside the District of Columbia. About 42,000 were engaged in research and development, more than half being in the Department of Defense and 20 per cent in the physical sciences. About 100,000 technicians were employed by the Federal Government, 35,000, including 21,000 engaged in nursing, being employed in the health fields;

12,000 were employed in biological and less than 5,000 in the physical sciences, and of the total, less than 15,000 were engaged in research and development, about half of whom were employed by the Department of Defense, mostly (86 per cent) as engineering or mechanics technicians.

National Health Service

OVERSEAS interest in the British National Health Service has led the Pharmaceutical Society of Great Britain to prepare an informative booklet which aims to identify the historical roots from which the present Service has grown, to explain a little of the complex financial basis, to describe the general structure, and, in more detail, the pharmaceutical services (*The British National Health Service: a Short Survey with particular reference to the Pharmaceutical Services*. Pp. ii+22. London: The Pharmaceutical Press, 1961. 5*s*.). Mention is also made of the main findings of some of the committees that have deliberated from time to time on the various problems affecting the Service. Although the booklet aims especially at supplying information to pharmacists and others overseas, it may also provide a suitable introduction to the intricacies of the profession for newly qualified pharmacists or pharmacy students in Britain. It should also serve as a refresher course for those pharmacists who, although familiar with the day-to-day forms and procedures of the Service as it affects them, are sometimes less sure about the general structure of which they form so integral a part.

The United Kingdom and the Common Market

UNDER the title *The Common Market and the United Kingdom* the Westminster Bank, Ltd., has issued an admirable concise guide to the European Economic Community and the possible effects on Britain of membership (Pp. 30. London: Westminster Bank, Ltd., 1961). After a brief introduction which notes the complications arising out of Britain's position in the Commonwealth, her obligations to the European Free Trade Area and the special problem presented by agriculture, the pamphlet describes the European Economic Community, its organization and progress and then seeks to assess the effects on the United Kingdom of entry into the Common Market, including the effects on industry, on agriculture and on the consumer.

The Polish Academy of Sciences

IN the *Review of the Polish Academy of Sciences* for January–March 1961 (No. 1, Vol. VI), W. Nowacki assesses the research plans of the Academy's agencies for 1961–65, and S. Zolkiewski the present state of the social sciences and the humanities in Poland. Besides B. Swietochowski's account of the scientific work of the Wroclaw Agricultural College, which includes a full bibliography, the *Review* includes notes on the several research centres for thermoenergetics, forestry research, pharmacological research and general theory of organization and on the Institute of Biochemistry and Biophysics and the Basic Raw Material Research Centre of the Institute of Physical Chemistry.

Nature Conservation in Western Malaysia

A SPECIAL issue of the *Malayan Nature Journal* has been prepared to mark the twenty-first anniversary of the Malayan Nature Society ("Nature Conservation in Western Malaysia", 1961. Edited by J. Wyatt-Smith and P. B. Wycherley. Pp. viii+261+44 plates. Kuala Lumpur: The Malayan Nature Society, 1961. Soft back, 12*s*. 6*d*.; hard back, 17*s*. 6*d*.). It contains forty-five articles by forty-one contributors dealing with such topics as the Malayan Nature Society, 1940–61; conservation and education; the Malayan Forest Department and conservation; river control and conservation in Malaya; conservation problems of Malaya's hill stations; conservation in Penang; nature protection in North Borneo; ferns in Singapore; limestone hills near Ipoh; Batu caves, Kuala Lumpur; cave archæology in Malaya; the distribution of elephant, rhinoceros, seledang and tapir in the King George V National Park, Malaya; the Shwe U Daung, a rhinoceros sanctuary in Burma; the Udjung-Kuolon Nature Park, Java; Mount Kinabalu, North Borneo; and the Bako National Park, Sarawak. There are also a number of articles dealing with wild-life conservation in other lands. E. J. H. Corner, now reader in taxonomy at the University of Cambridge, and formerly assistant director of gardens, Straits Settlement, Singapore, contributes a stimulating introduction.

Insects as Social Animals

THE fourth congress of the International Union for the Study of Social Insects was held in Pavia during September 9–14, at the invitation of the president of the Italian section of the Union, Prof. Carlo Jucci. Some two hundred people took part and 72 papers were read. There were symposia on endocrinology, caste differentiation, symbiosis and gregarism, and sections devoted to bees and wasps, ants and termites. Among the contributors were Prof. P.-P. Grassé (evolution of symbiosis in termites), Prof. C. Jucci (comparative endocrinology of social insects), Prof. M. Lüscher (hormonal regulation of development in termites), Prof. K. Gösswald (acceptance and rejection of radioactive markers by solitary and social insects), and Prof. J. B. S. Haldane (statistical analysis of some data on ant and wasp behaviour). A well-arranged exhibition was another feature of the congress. This included historical documents relating to earlier workers on social insects—Grassi, Silvestri, Forel and others; scientific exhibits ranging from photographs of African ant-galls and Australian termite mounds, to anatomical preparations; and a section on control measures, which included exhibits showing the progress of termite control in Italian libraries, and the successful introduction of the wood ant, *Formica rufa*, for the biological control of pests in Italian forests. The proceedings of the congress are to be published in the series *Symposia Genetica* of the L. Spallanzani Zoological Institute, University of Pavia.

Leucocyte Migration in Inflammation

Sir Howard Florey and L. H. Grant, in an article appearing in a recent issue of the *Journal of Pathology and Bacteriology* (82, No. 1; July 1961), report investigations of the passage of leucocytes through the walls of blood vessels inflamed by ultra-violet light in rabbit tissues using electron microscope techniques. No clear morphological evidence was obtained that the surface of the endothelium became 'sticky', although occasionally electron-dense material was seen in relation to the endothelium. The leucocytes penetrate the endothelium by thrusting out pseudopodia, possibly down cell junctions, and passing through until they reach the basement membrane, collagen fibres and pre-

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endothelial cells. It would appear that they then usually move parallel to the endothelium until they gain exit to the surrounding connective tissue. The granules of the polymorphs do not seem to undergo any changes during migration. Monocytes behave in the same way as polymorphs. Vacuoles of unusual appearance are seen in the endothelium after ultraviolet stimulation but not after mechanical 'insult'.

Chalk River Atomic Energy Instrumentation Conference

THE complete set of five parts of the proceedings of the Sixth Tripartite Instrumentation Conference, which was held at Chalk River, Ontario, during April 20–24, 1959, is now available (Edited by J. E. Woolston and S. J. Townsend. Part 1: *Reactor Instruments*. Pp. xi+214. 5 dollars. Part 2: *Radiation Dosimetry*. Pp. xi+145. 3 dollars. Part 3: *System and Component Reliability*. Pp. viii+19. 1 dollar. Part 4: *Instruments for Nuclear Physics*. Pp. xi+212. 5 dollars. Part 5: *Radiation Detectors*. Pp. ix+76. 2 dollars. Chalk River, Ontario: Scientific Document Distribution Office, Atomic Energy of Canada, Ltd., 1960. 15 dollars the set). The participants consisted of members of the United Kingdom Atomic Energy Authority, Atomic Energy of Canada, Ltd., and various scientific and industrial laboratories in the United States of America. Some of the articles are abbreviated, but the discussions are given in full. Part 1 (thirty-one contributions) deals with reactor instruments and includes brief reviews of reactor instrumentation practice in the United Kingdom and at Savannah River. In the first three articles in Part 2 (twenty-nine contributions), which is concerned with radiation dosimetry and health instruments, descriptions are given of the health-physics instrumentation at the Brookhaven National Laboratory and at the Hanford Atomic Products Operation, Richland, and of radiation dosimetry at Chalk River. Part 3 (five contributions) on system and component reliability includes a summary of the reliability performance of equipment at Harwell during 1953–56, and an analysis of the component failure at Chalk River during 1956–59. A wide range of electronic, including transistorized, equipment is covered in Part 4 (thirty-three contributions), which deals with instruments for nuclear physics, and in Part 5 (fourteen contributions), on radiation detectors, various forms of ionization chambers, fission chambers, scintillation counters and semi-conductor radiation detectors are described.

Artificial Earth Satellites

THE memoir, "Artificial Earth Satellites", recently issued by the Radio-Electronics Section of the British Astronomical Association (**39**, No. 2; August 1961. Pp. viii+160. Hounslow West, Middx.: British Astronomical Association, 1961. 20*s*.; 3 dollars), is divided into two sections. The first section (contributed by J. Heywood) is devoted, first, to an introductory survey of Earth satellites; and secondly, to a historical review of the radio measurements made by members of the British Astronomical Association and Radio Society of Great Britain on *Sputniks* 1 and 2. The second section (contributed by various authors) is concerned with the techniques of visual and photographic satellite observation, the use of charts for the prediction of satellite positions and the graphical derivation of apparent tracks for satellites. The memoir, compiled and edited by J. Heywood, should be of interest to all amateur observers of artificial Earth satellites.

University News: London

THE title of professor of theoretical physics has been conferred on Dr. P. T. Matthews, in respect of his post at the Imperial College of Science and Technology. The following have been appointed to readerships: Dr. K. A. Kermack, vertebrate palæontology at University College; C. H. Lack, bacteriology at the Institute of Orthopædics; Dr. J. E. Prentice, geology at King's College; Dr. M. Schacter, physiology at University College; Dr. Gordon Smith, virology at the London School of Hygiene and Tropical Medicine; Dr. Maynard Smith, zoology at University College; Dr. G. L. Watson, mathematics at University College.

The Research Report 1958–61 of the City and Guilds College gives a very readable account of the work carried out in the five engineering departments of the Imperial College of Science and Technology—Aeronautics, Chemical Engineering and Chemical Technology, Civil Engineering, Electrical Engineering and Mechanical Engineering (Pp. v+96. London: Imperial College of Science and Technology, City and Guilds College, 1961). While the account makes clear the importance of the contribution of the College to present-day technological advances, it is left for the reader who is interested in particular researches to approach the relevant Department direct for further information. No names of those responsible for the various researches are given, nor is a list of published papers included.

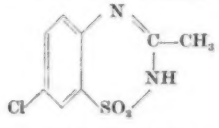
Announcements

THE Imperial Forestry Institute at Oxford has been re-named the Commonwealth Forestry Institute.

THE next symposium of the Society for the Study of Development and Growth will be held during June 24–27, 1962, at "Asilomar", Pacific Grove, Monterey Peninsula, California. The subject of the symposium will be "Cytodifferentiation and Macromolecular Synthesis".

THE Council for Nature is organizing two seven-day courses on natural history at its Brantwood Centre, Coniston, Lancs, during May 12–19 and May 19–26. The courses are intended primarily for amateur naturalists. Further information can be obtained from Stanley Jeeves, Council for Nature, Brantwood, Coniston, Lancs.

ERRATA. The structural formula of 3-methyl-7-chloro-1,2,4-benzothiadiazine-1,1-dioxide (*SRG* 95213) was misrepresented in the letter entitled "A Non-diuretic Benzothiadiazine with Anti-hypertensive Properties" which appeared on p. 176 of the October 14 issue of *Nature*. The correct formula is:



IN the communication entitled "Preparation and Determination of Sulphosalicylo-soluble Proteins using Tannin", by Prof. W. Mejbaum-Katzenellenbogen *et al.*, in *Nature* of October 21, p. 262, par. 2, last line, for "an appropriate conversion factor should be used" read "no conversion factor should be used".

THE WATER RESEARCH ASSOCIATION

NEW RESEARCH STATION

THE Water Research Association (director, Dr. R. G. Allen) invited its members on September 20 to inspect the permanent Research Station on the River Thames at Medmenham, in Buckinghamshire, into which it moved earlier this year. The Association was founded by water undertakings and is now in receipt of grant-aid under the scheme for industrial Research Associations operated by the Department of Scientific and Industrial Research. Previously it had been in temporary accommodation at Redhill, and with the move into specially designed buildings on a site where there is a plentiful supply of raw water, and provided with appropriate facilities for experimentation, it can be seen that the organization has now attained its full stature as an established Research Association.

The removal to new laboratories made it possible both to extend the scope of the research on hand and to begin programmes in new fields. The internal organization was expanded to comprise the following eight divisions: chemistry; physics; biology; hydrology; plant process; information; workshop services; administration. Thus there are now staff and facilities for work on every technical aspect of providing potable water.

Perhaps the most interesting structure in the new buildings is the Pilot Plant Laboratory, which has a total floor area of about seven thousand square feet, with a maximum roof height of thirty-six feet. This laboratory is intended primarily for the testing of equipment and techniques on the industrial scale; raw water is brought in from the River Thames and the construction and fittings are designed specifically for such work.

Specialized laboratories include those for physics, and for physical chemistry, general chemistry, coagulation chemistry, chemical instruments, microbiology and hydrology. There is a well-equipped machine shop. The library is being enlarged with the object of maintaining a unique collection of the literature relating to certain technical aspects of the water industry which are not indexed together elsewhere.

Chemistry Division

In the Chemistry Division the main work has been on the use of coagulation in water treatment. In this commonly used chemical process the fine suspended particles of clay which cause turbidity in water are made to coagulate into a floc of larger particles by the addition of a coagulant such as aluminium sulphate, and are then removed comparatively easily by settlement.

This investigation has thrown a completely new light on the mechanism of coagulation. It has been found that the range of values of *p*H in which the coagulation process is most efficient in removing turbidity corresponds to that in which the hydrolysis product is most rapidly flocculated, that concentrations of various coagulants which are equivalent in terms of aluminium concentration are not equivalent in terms of coagulant efficiency, and that there is at least a rough relationship between the relative coagulant efficiency and the amount of hydrolysis product that is precipitated immediately on reaction of the coagulant with water. This suggests that the mechanism of the clarification of turbid water is not coagulation in its true sense; the only coagulation that takes place is that of the hydrolysis product, and the clay particles which constitute the turbidity are carried down in the mass of flocculating hydroxide particles. The precise nature of the interaction between the clay and the hydroxide is not yet clearly understood, but is being investigated.

A number of coagulants have now been studied in some detail, and other coagulants and materials assisting the coagulation process are also being evaluated.

Coagulation processes are also used for the removal of colour from water. To provide the quantities of the colouring matter (complex organic acids derived from soil humus) required for research, a technique has been developed in which this material can be isolated from raw Thames water at rates of flow of up to 100 gallons per hour. It is proposed in the near future to begin isolating the organic colour from a number of raw water sources in addition to that on the site, and to study the way these materials behave in flocculating systems.

An analytical section has been established within the Chemistry Division, and is making a systematic study of methods used in the analysis of potable waters. This section will investigate new techniques for the measurement of every aspect of water quality, and this experience will be of great value if eventually a water quality network is established in Britain, similar to that which operates in the United States of America.

Physics Division

The Physics Division is concerned with all the physical aspects of water distribution. Its principal research programmes at present relate to the application of plastic materials to the construction of water mains and service pipes, to methods of instrumentation (particularly for the detection of leaks) and to mathematical analysis of flows and pressures in water distribution networks.

In an investigation on plastic pipes it is hoped to establish optimum design criteria for long-term service. Plastics react to variations of stress and temperature in a more complicated way than iron and steel, and as their long-term strengths are not precisely known, deliberately conservative ratings are now being used. Progress has already been made towards determining the long-term effect of variations of pressure in plastic water-distribution mains, employing accelerated tests, and the present programme relates to the measurement and specification of impact strengths. The impact resistance must of course be high enough to withstand reasonable shock loads in transit, when being laid, or when other services are being installed in the ground alongside.

It is estimated that leakage from water distribution systems in Britain exceeds 10 per cent of the

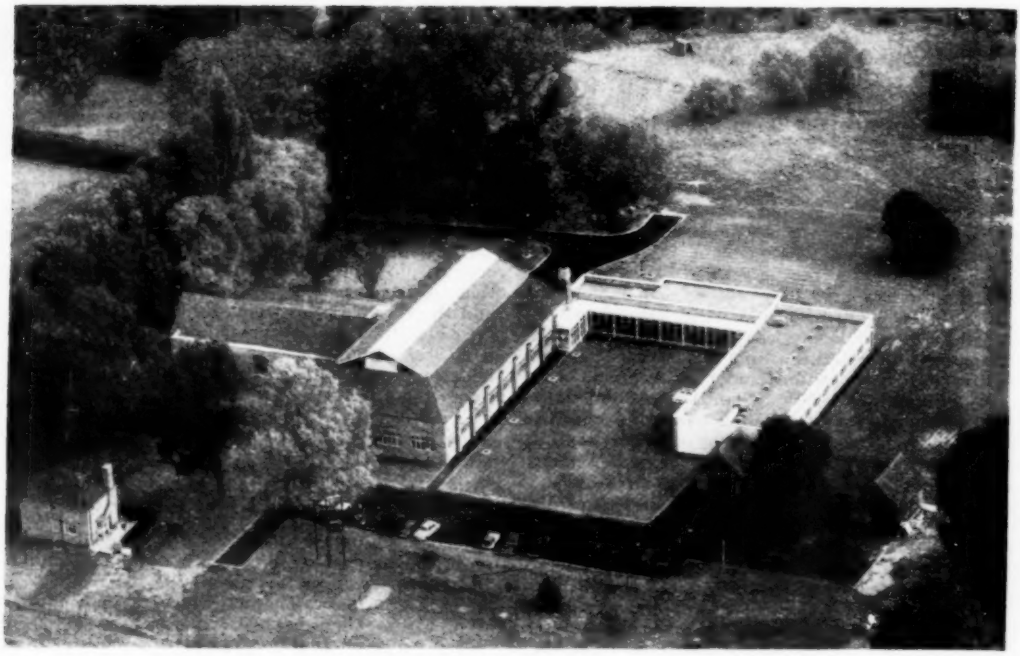


Fig. 1. The new Research Station of the Water Research Association, at Medmenham, near Marlow, Buckinghamshire. The grounds extend nearly to the River Thames, from which water is taken for experimental purposes

input, and a strong economic demand exists therefore for a device which will accurately locate leaks from buried water mains. The object of the programme in this respect is to develop a telemetering system in which an instrument carrier will be drawn along inside the pipeline and will transmit readings to an observer on the ground surface. Plunger devices (termed 'ferrets', 'go-devils' or 'pigs') which are driven through distribution mains by the fluid pressure are already in use for cleaning and other purposes, and such devices would also be suitable for carrying instruments. The first phase of the programme has therefore been the development of suitable signalling equipment, and devices have now been demonstrated which transmit a magnetic signal from a small piece of equipment inside a buried pipeline of any material including iron and steel, through the earth or other top filling, to light-weight portable receiving equipment.

While the work on the development of a complete telemetering system continues, the method of transmitting a signal from inside a buried pipeline is being put to good use in the design of a device to detect the position of a 'ferret' in service. This has now reached the prototype stage. An electro-magnetic beacon is attached to the 'ferret', so that its position can be found by moving the receiving equipment until the signal is loudest. It has been a major objection to the use of 'ferrets' that if they should stop in the pipeline it might be a very difficult matter to find and recover them, and a reliable 'ferret' detector should encourage their wider use.

As areas of water supply are extended, and rising demand brings many of the supply mains nearer their limits of capacity, it becomes increasingly important that it should be possible to calculate pressures and flows rapidly and accurately under existing and postulated conditions of supply and demand. Such calculations are altogether too time-consuming to be done by hand, and investigations have therefore been made of the use of both analogue and digital computers to produce methods of rapid and precise computation.

Plant Process Division

The Plant Process Division was set up when the Association had moved to its new establishment. The present programme is as follows: to investigate existing water-treatment processes; to develop from the findings of the Chemistry Division new processes which may be applied to full-scale waterworks plant; to investigate particular problems which may occur in the plant of members of the Association.

The equipment which is at present being designed will occupy a large part of the Pilot Plant Laboratory, and will include two treatment processes, one as a standard of reference. It will be large enough to ensure that the processes developed in it can be transferred to full-scale plant without further difficulty, while still being small enough to be flexible in operation. This plant will use raw water from the Thames at a maximum rate of about a thousand gallons per hour.

Hydrology Division

The study of hydrological problems is the responsibility of another newly established Division. The work of the Water Research Association in this field is part of an integrated national programme, and its present aims are: to encourage the improvement, both in quality and quantity, of hydrological measurements made by water undertakings; to advise the water undertakings in membership on ways of using their own hydrological data; to co-operate in the

scientific study of evaporation and rainfall measurements in upland catchment areas of the British Isles.

The Hydrology Division is devoting its main attention at present to surface waters. The water industry is immediately interested in calculating effective reservoir capacities, and in the effects of different types of land use on water yield. Several continental countries and the United States of America have made considerable progress in this respect and their results, although not directly applicable to the very different conditions in Britain, suggest a number of ways by which substantially increased yields might follow if the necessary data were determined and applied. The research aspects of the work of the Hydrology Division work are designed to assist in this.

In addition, since 30 per cent of the raw water taken by water undertakings in the British Isles comes from underground sources, these must be assessed as regards their long-term yield in terms of infiltrating rainfall. Natural replenishment by this means is a very slow process, but artificial replenishment by pumping from surface water sources offers storage at low capital cost. This method is already in use in Sweden, Germany, The Netherlands and the United States of America; the Association's programme provides for research to assist in collecting reliable data and overcoming technical difficulties.

Biology Division

The biological aspects of the water supply process are clearly of the utmost importance, not only because biological purity is required equally with chemical purity but also because biological as well as chemical processes are employed in water purification.

The Biology Division has only recently been established, and is still engaged on a preliminary examination of the problems. It is expected that its first programmes will be concerned with aspects of water sterilization, with the development of faster techniques for bacteriological examination and with the control of algae in stored waters.

Information Division

The objects of the information services are to see that new information from all sources is readily available to members, to provide assistance with day-to-day problems where the necessary information already exists, and to maintain communication with the water industry, other research establishments and other organizations with appropriate interests throughout the world.

In addition to the material supplied to staff and members by the library, numerous technical inquiries from members are answered. The staff of the Association is in a position to accumulate extensive experience of such problems, to maintain contact with specialists and to keep abreast of the published information.

The problems presented are normally within the experience of the technical staff of an undertaking but outside their special province. They cover a very wide range of topics; a typical selection might include complex cases of corrosion, attacks by insects (even on polythene water-supply pipe), the infestation of water supplies by various organisms, the chemical contamination of supplies, and such practical problems as the protection of reservoirs from birds.

In addition to its technical papers the Association publishes a periodical, *Water Research News*.

The Future

In its recent annual report, the Council of the Water Research Association comments: "It is now apparent that considerable changes will be required in the nation's water systems if the rapid increases in agricultural and industrial demands are to be met everywhere. The techniques of every stage of the water supply process are open to review, and a large part of the work must properly fall on the Water Research Association".

A visitor to the Water Research Association will realize that this consideration underlies all the planning at the new Research Station.

MUSCLE RECEPTORS

THIS year the University of Hong Kong, as part of its golden jubilee celebrations, held six symposia during September 11–16. One of these, under the chairmanship of Prof. Ragnar Granit (Stockholm) was on muscle receptors. It was organized by Prof. D. Barker, professor of zoology. There were about thirty participants, who represented both the physiological and histological aspects of work on receptors in mammalian muscle. The muscle spindle was considered from many angles and the papers, which ranged from accounts of the exacting work of electrical recording and single nerve fibre stimulation to details of the intricate structure of spindle innervation were given to full audiences and provoked lively discussions.

Prof. Granit opened the proceedings with a summary of much of the earlier work and a statement of some of the outstanding problems. A special lecture by Sir John Eccles (Canberra), who was unable to be present, on the "Central Connections of Muscle Afferent Fibres", was read by Prof. A. K. McIntyre (Otago, New Zealand). In the papers and demonstrations that followed, evidence was given of new advances which we may expect to see developed further in the future. H. Shimazu and T. Hongo (Tokyo) directed attention to brain-stem influences on the motor supply to muscle spindles, while E. Eldred (California) spoke of cerebral influences. McIntyre considered that any discharges passing up muscle nerves and reaching the cerebrum probably came from Pacinian corpuscles and joint receptors and not from spindle primary endings. Y. Laporte (Toulouse) described elegant work in which both the primary and secondary afferent endings in a single spindle could be subjected to controlled stimulation of the spindle motor nerves and the responses compared. C. Eyzaguirre (Salt Lake City) spoke of spindle motor innervation and described how some of the intrafusal muscle fibres were actually seen to contract slowly. I. A. Boyd (Glasgow) gave a graphic account, with many beautiful colour slides, of the whole structure of muscle spindles in the cat, based on de-afferented and de-efferented material and much work on nerve fibre spectra. He directed particular

attention to the possibility of a double motor innervation. D. Barker (Hong Kong) and his co-workers, N. K. Chin, M. N. Adal, M. C. Ip and M. Cope, also described much detailed work on the structure, nerve spectra and distribution of spindles in cat muscles. It became obvious that there are points of great interest to both physiologists and histologists still needing to be settled about the complexity of the motor innervation of spindles.

The mechanisms by which sensory endings initiate electrical discharges were considered by C. C. Hunt (Salt Lake City), using the simpler Pacinian corpuscle. The electron micrographs shown by M. C. R. Merrillees (Melbourne) gave an insight into the ultrastructure of both spindle and tendon organ endings and their relation to underlying tissues. A. S. Paintal (New Delhi) directed attention to the less well-known muscle receptors, with small nerve fibres, which probably subserve pressure and pain. K. S. Lim (Indiana) also spoke of the responses of these endings. Other papers dealt with pharmacological studies of spindles (J. E. Pascoe, London, and H.-D. Henatsch, Göttingen); spindle numbers and distribution (Eldred); differentiation of primary and secondary ending discharges (S. Cooper, Oxford); the potentiation of motoneurones by spindle discharges and also human experiments on reflexes involving muscle receptors (S. Homma, M. Kano and K. Takano, Chiba, Japan).

The ideal conditions under which the symposium was held both in the Department of Zoology and in the beautiful surroundings of Hong Kong gave many opportunities for discussions in small groups which did much to bring to light problems of structure and function that may be solved by mutual efforts of the workers in the two fields.

The Hong Kong University Press plans to publish the Proceedings early in 1962. SYBIL COOPER

CHEMOTHERAPY OF VIRUS DISEASES

At a meeting of the Fine Chemicals Group of the Society of Chemical Industry held in the Wellcome Foundation on October 6, the subject under discussion was research on the chemotherapy of virus diseases. There are two ways in which this subject can be approached. What might be called the rational approach requires an investigation of the essential components of virus multiplication with special emphasis on those steps which could be readily inhibited. Thus, many substances are known that will inhibit the synthesis of viral nucleic acid or viral protein or that will block the supply of energy required for virus multiplication. The problem is not how to inhibit virus growth but how to inhibit it selectively, without at the same time damaging the host cells. The second approach, the empirical one, seems to have been the favoured approach, and one which has had more success so far.

Dr. A. Isaacs (National Institute for Medical Research) presented the first paper, on interferon. Interferon was first found during an investigation of the phenomenon of viral interference, in which it seems to play an important mediating part. Further investigations suggest that it may also play a part in the immune processes that lead to recovery from virus infections.

Interferon is a protein of molecular weight 63,000 which is produced by cells of a number of different vertebrates in response to infection with a large number of different viruses. Its antiviral activity is usually more apparent in cells of the animal species in which it was made. However, it is active against a wide range of animal viruses although there are differences among viruses in their sensitivity to interferon. It does not prevent adsorption or penetration of virus but it inhibits the replication of viral ribonucleic acid. This probably results from inhibition of an oxidative process of the cell which supplies the energy for viral synthesis. The inhibition seems to affect viral synthesis much more than normal cellular syntheses, however, since human thyroid cells can divide at a rate not grossly different from that of normal cells in the presence of a large amount of interferon.

There is growing evidence that antibody may play a less important part in the processes of recovery from virus infections than has been thought hitherto, and that interferon may play a more important part. This was shown first by experiments in chick embryos of different ages, in which recovery from virus infections is found to be closely related to development of sensitivity to interferon. Secondly, persistence of virus in the lungs of mice of different ages was found to be inversely related to the production of interferon in these animals. Thirdly, two ways of inhibiting the interferon mechanism *in vitro*, namely, increased oxygenation and treatment with cortisone, both have a detrimental effect on the course of virus infections *in vivo*. These findings point to the conclusion that interferon may play an important part in our ability to recover from virus infections and they suggest that it might be possible to assist natural recovery from virus infections by giving interferon therapeutically. This has been carried out successfully in some virus infections of animals and it is hoped that preliminary trials of its action in man will begin shortly.

The second paper was given by Drs. R. Hull and E. W. Hurst (Imperial Chemical Industries, Ltd.) on structure activity in various heterocyclic compounds.

Material tested for possible antiviral activity was obtained from products synthesized for other biological assays, from the synthesis of analogues obtained in the course of following up an antiviral lead already found in the department or elsewhere, and from the synthesis of possible antimetabolites to viral nucleic acid. Heterocyclic compounds constituted the largest section of organic compounds tested and a review was given of structure–activity relationships that had been found in the acridines. 'Mepacrine' was the most active and showed antiviral activity against equine encephalomyelitis, Rift Valley fever and louping ill viruses.

In evaluating experimental work it was important to take into consideration the complex of cell and virus that was studied. Examples were given of compounds which reduced the growth of viruses in the chick embryo but which were not appreciably

active in the mouse. On the other hand, 'Mepacrine', which was active against equine encephalomyelitis virus in the mouse and adolescent rat, was inactive against this virus in the chicken, guinea pig, rabbit and monkey.

Work on simple antimetabolites, in which the furan ring had been substituted for the ribofuranoside moiety in the nucleoside, had led eventually to certain tetrahydropyrimidines which showed activity against viruses of the psittacosis-lymphogranuloma-trachoma group both in the chick embryo and in the mouse. One, 17,025 [5-methoxycarbonyl-6-methyl-4-(5-nitrofuryl)-2-oxo-1,2,3,4-tetrahydropyrimidine] which was sparingly soluble in water, had very low toxicity and was both effective and non-irritant when given by the intramuscular route. It showed, weight for weight, rather less than one-tenth of the activity of chlorotetracycline. Its clinical use might be envisaged (for example, against trachoma) when it was desirable to control an infection by infrequent parenteral therapy rather than by prolonged topical application or by frequent oral dosing.

The third paper, by Drs. D. J. Bauer and P. W. Sadler (Wellcome Laboratories), was concerned with the antiviral action of derivatives of isatin β-thiosemicarbazone on viruses of the pox group. These compounds are known to show antituberculous activity and they were later shown by American workers to have some antiviral action against vaccinia virus. However, the latter work was not followed up until the group at the Wellcome Laboratories commenced detailed investigations of a number of derivatives of isatin β-thiosemicarbazone on a number of different members of the pox virus group. Perhaps the most striking finding has been the selectivity of action of these compounds. Thus, isatin β-thiosemicarbazone and some of its derivatives are very active against vaccinia but have no activity against ectromelia virus; conversely, isatin β-4′ : 4′-dialkylthiosemicarbazone and related compounds are highly active against ectromelia but not at all active against vaccinia virus. This specificity should provide an important clue to the mode of action of these compounds. To the authors it suggested that these compounds were not acting on some cellular enzyme required for viral synthesis, but that they were acting directly on the virus itself.

A most interesting aspect of this work is the finding that *N*-ethylisatin β-thiosemicarbazone, in doses of 0·03 and 0·015 mgm. twice daily for five days, protected infant mice (less than six days old) against fatal infection by the viruses of alastrim and variola major. Dr. Bauer discussed at some length the question of the importance of the treatment of smallpox in these days of vaccination and he concluded that there was a strong case for trying out these compounds in man and that it was reasonable to expect that a specific anti-smallpox drug would be in use within the not too distant future.

ALICK ISAACS

PHOSPHOLIPIDS AND SULPHOLIPIDS

DR. M. MACFARLANE, joint chairman with Prof. D. D. Eley of the joint meeting of the Biochemical Society and the British Biophysical Society on "Phospholipids and Sulpholipids", which was held at the School of Pharmacy, University of London, during October 5–6, underlined its significance by a quotation from the Macleans (1927)[1]. "When we consider the obscurity in which the chemistry of the phospholipids has been shrouded, it is easy to understand that many of the properties and functions ascribed to these bodies are based on little more than imagination." Thirty years later imagination remains in plenty, but an immense amount of accumulated factual evidence was presented at the meeting. The chemical, physical and physico-chemical problems surrounding phospholipids challenge all scientists interested in the structure and functions of the living cell.

With the advent of recent analytical procedures involving chemical[2,3] or enzymatic hydrolysis, paper and silicic-acid chromatography[4], the compositional detail of many animal and plant tissues is progressing fast. Consequently, the phospholipid chemist of to-day recognizes phosphatidylglycerols ; phosphoinositides; the classical ester phosphatides having either serine, ethanolamine or choline as the nitrogenous base; the plasmalogens, being analogous to the phosphatides, but with an aldehyde in place of a fatty acid; the sphingomyelins, the complex phosphoinositols and finally the lysophosphatides. Among many most recent compositional details reported at the meeting was the observation by Dr. G. R. Webster that the ethanolamine base in brain white matter is predominantly present in plasmalogen instead of the more usual phosphatidyl ethanolamine. Dr. E. Lederer, withdrawing earlier claims, pointed out that mycobacteria do not appear to contain any nitrogenous base phospholipids but do yield mixtures of phosphatidyl-inosito-mono, di- and tri-mannosides. Of great interest, however, was his report on the structure of the phosphatidyl-inosito-dimannoside, and of his proof that the 6-*O*-α-D-mannopyranosyl-α-D-mannopyranose is inositol linked, the dimannosides alone being almost as effective as *BCG* vaccine in the protection of animals against tuberculosis.

In plant chloroplasts the major anionic lipids are phosphatidylglycerol and the sulpholipid, 6-sulpho-α-D-quinovopyranosyl-(1 → 1′)-2′ : 3′ diacyl glycerol. The precise formulation of the latter compound has been established by Dr. A. A. Benson in an elegant analytical procedure. The presence of lipid lamellæ in plant chloroplasts and the high-rate of incorporation of carbon-14 dioxide, phosphorus-32 labelled phosphate and sulphur-35 labelled sulphate ions into the anionic lipids during photosynthesis points to at least two functions of phospholipids—namely, interfacial orientation with concomitant orientation of adjacent molecules, such as enzymes, and involvement in translocation of metabolic products.

With commercially available gas chromatography apparatus, each phosphatide can now be examined in terms of its fatty acid composition. This further stage in the dissection of phospholipids was reported on by Dr. G. M. Gray, who compared the mean fatty acid composition of normal tissue phospholipids with those from Landschutz ascites tumour cells. Surprisingly, and perhaps of fundamental importance, the tumour cell phospholipids showed far less variation in the kind of fatty acid acylated. For example, stearic is the predominating saturated acid in all tumour phospholipids, thus differing from normal

tissues in which palmitic acid is the major saturated acid of phosphatidyl choline and choline plasmalogen.

Prof. L. L. M. van Deenan and his colleagues at Utrecht rightly argued that a better understanding of the physical properties to be attributed to the fatty acids and to their particular position in the phosphatide molecule would clarify the biophysical properties of the phospholipid. Reporting a remarkable programme of syntheses involving re-acylation of L-α glyceryl phosphoryl choline, with fatty acids of varying chain-length, Prof. van Deenan was able to contribute experimental results obtained from his semi-synthetic material and relate it to many of the chemical and biophysical aspects covered during the meeting. Perhaps the most significant advance so far resulting from the use of these re-acylated phosphatides has been to establish beyond doubt that the phospholipases *A* of snake or bee venoms only release the fatty acid from the β position.

Combining biochemical and biophysical techniques, Dr. A. D. Bangham and Dr. R. M. C. Dawson presented substantial evidence to suggest that the activation of at least two phospholipases is controlled by the electrokinetic properties of the lipid/water interface. The ζ potential of lecithin suspensions was varied either by adding insoluble amphipathic molecules, for example, docosanyl pyridinium bromide or dicetyl phosphoric acid to the lecithin or by the addition of multivalent ions, for example, calcium ions or ferricyanide ions, to the bulk aqueous phase. Such experiments showed that *Penicillium notatum* phospholipase requires micelles having a net negative (> 15 mV.) ζ potential before hydrolysis of the lecithin occurred. Calcium, uranyl and thorium ions, if present, as multivalent gegen ions, inhibited the system. The phospholipase *C* (α toxin) of *Clostridium perfringens*, however, required a positively charged lipid interface and required either the addition of amphipathic cations to the lecithin, or divalent calcium or magnesium ions to the bulk aqueous phase. That these interactions are confined to the lipid-water interface was demonstrated by following the hydrolysis of unimolecular films using lecithin highly labelled with phosphorus-32. The ability of phospholipase *C* (α toxin) to hydrolyse phosphatidyl ethanolamine, but only in the presence of lecithin, confirms earlier work and fits in well with the hypothesis that lecithin, being a surface-active zwitterion, can dilute the high net negative charge of a pure phosphatidyl ethanolamine micelle with ionically neutral molecules, thereby permitting the negatively charged enzyme to approach the micelle. The adjustment of the net charge of lipids by admixture of lecithin may well be an important feature in a variety of biological systems, for example, blood coagulation, fat absorption. Endorsing the importance of a definitive lipid/water interface for the activation of phospholipase *C*, van Deenan reported that synthetic phosphatidyl cholines prepared with C_2 or C_4 fatty acids were not hydrolysed and could not be shown to have any lamella structure in electron microscopic preparations.

The present-day biophysical interest in phospholipids naturally centres around the structural arrangement of such molecules in various solvents—and in particular in water. The accepted interpretation of the results obtained by X-ray diffraction, light scattering and with polarized light, is that most phospholipid mixtures consist of concentric layers of bimolecular leaflets intercalated with water. The smallest repeating unit of mixed phospholipids in the presence of protein has recently been examined and the precise significance of the electron opaque lines of methacrylate embedded, osmium-fixed material discussed by Stoekenius, Schulman and Prince[8]. Their evidence, together with that of Finean[6], strongly suggests that the smallest unit membrane recognizable in model lipid membranes is a bimolecular leaflet covered on both sides with protein—a structure postulated by Danielli nearly thirty years ago and recently presented by Robertson[7] as a structural entity in some biological cell components.

Of particular interest to the biologist is the intermolecular arrangement of the phospholipids and sterols in the plane of any unit membrane or film. Dr. D. G. Dervichian and de Bernard[8] have already shown that in monolayer studies, lecithin forms molecular condensations with cholesterol, and Willmer[9] has recently indicated how such mixtures might give rise to a variety of mosaic patterns, conceivably controlling the permeability of membranes or in facilitating the absorption of specific proteins (for example, gonadotrophin).

The precise orientation of the ionic groups of the phospholipid is at present a matter of some controversy, but the concensus of opinion is that with pure phospholipids the charged groups lie in a nearly level plane at the water interface. Finean[10], however, has presented evidence that cholesterol might realign the base of a phospholipid away from the water; in so doing, local areas of phospholipid surfaces might present net negative ζ potentials.

As it is now possible to prepare large quantities of chemically pure, although inhomogeneous in fatty acid, lecithin, this substance has been studied extensively in terms of its conductivity, viscosity and micelle formation. Drs. P. H. Elworthy and D. S. McIntosh, examining the light scattering of lecithin, found that the micellar weights increased as the polarity of the solvent decreased. They also concluded that in their series of solvents—ethanol, *n*-butanol and *n*-hexanol—the polar groups were probably hidden, while the hydrocarbon chains protruded outwards into the solvent. This result is of great interest when it is remembered that lecithin exists as very large micelles in water and with the polar groups outwards.

The behaviour of fairly concentrated sols of lecithins in water with salt solutions has formed the basis of a study by Dr. L. Saunders and was reported to the meeting. He finds that a film of some measurable mechanical strength forms at the sol/salt interface and that this film has some of the permeability characteristics of cell membranes. Presumably the intermicellar channels restrict the diffusion of divalent and, to a lesser extent, monovalent ions.

Finally, it must be remembered that phospholipids and sulpholipids are integral parts of living cells and as such are in dynamic equilibrium with metabolic and structural processes. Isotope incorporation studies have repeatedly shown that certain phosphatides can exhibit high rates of turnover in cells undertaking active secretive or ingestive functions[11]. L. E. Hokin and M. R. Hokin, for example, reported how the salt gland of certain marine birds rapidly incorporated phosphorus-32 when the gland was stimulated with acetyl choline—the normal physiological stimulus. Their evidence is suggestive that in this instance sodium transport is coupled to the renewal of phosphate in phosphatidic acid, a process which appears to be catalysed by the cyclic action of

diglyceride kinase and phosphatidic acid phosphatase. The questions raised during the course of this meeting suggest that it would be foolish to expect a complete understanding of the function of phospholipids even within the next thirty years. A. D. BANGHAM

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BUILDING RESEARCH

THE annual report for 1960 of the Building Research Board of the Department of Scientific and Industrial Research (Pp. 99. H.M.S.O., London. 7*s.* 0*d.*) is written and illustrated with the clarity which has characterized previous reports, and provides a convenient summary of the very diverse activities of the Building Research Station.

Before a new building material can be used with confidence, information is needed on many aspects of its behaviour over long periods of time, and the devising of suitable accelerated tests is a major problem in this field of research. The present report describes such a test for the weathering of polyester roofing sheets reinforced with glass fibre. Work is in progress on the behaviour of rain-water goods made from various plastics; the chief problem here appears to be lack of colour stability.

Another group of materials, lightweight aggregates for structural concrete, poses many problems including mix design, bond strength, moisture movement, and corrosion of reinforcement.

Work in this field, begun in 1957, is still in progress, and aims to provide the basis for a future code of practice.

Like most similar organizations, the Building Research Station is often asked to solve a problem within a few months. Their experience has shown that "superficial short-term examination of problems is apt not to be rewarding". Unhappily, the converse is not always true, and one feels sympathy for the workers on stone preservatives who report, after five years investigation, that "no 'stone preservative' treatment has yet served its purpose well enough to merit commendation. Some have done more harm than good . . . nothing of proven value has emerged . . .".

Another important group of investigations is concerned with the economics of building construction and maintenance. A survey of 1,000 post-war houses in Scotland has shown that certain non-traditional forms of construction lead to abnormally high maintenance costs, especially in conditions of severe exposure. Prefabricated systems have a tendency to leave small quantities of work to be completed by traditional methods, at disproportionately high cost.

The structural designer will be interested in the development of realistic design methods based on more comprehensive data than those now available. New surveys of actual floor loads and snow loads on buildings are now in hand, and the problems of wind loading on tall buildings are also receiving attention.

An important study of composite action in buildings is in progress. Attention to the interaction of beams and slabs, and of walls and structural frames can make more difference to frame design than can the most elaborate frame analysis.

The Building Research Station pioneered soil mechanics research in Great Britain, and is continuing the investigation of pile foundations. It would appear from results quoted in this report that the ability of deep cylinder foundations to carry load by both shaft friction and base reaction is still in some doubt.

This important conclusion appears to be based on a limited series of tests on a laboratory model, and it would be a great help to readers if statements of this nature were accompanied by references to the list of publications at the end of the report. At present it is not at all easy to relate the conclusions reported to the publications giving details of the original work.

The contents of the present annual report cover a very wide field, and this arbitrary selection of topics can do little more than indicate the diversity of matters treated. No mention has been made, for example, of the interesting work on the equatorial comfort index for tropical buildings, or the effect of various construction methods on the earth pressures on buried service pipes. In both cases an attempt is being made to replace the present trial-and-error approach by a logical theory developed from observed facts.

This report should be of interest to all who design buildings or organize their construction.

R. PAUL JOHNSON

INDUSTRIAL RESEARCH AND DEVELOPMENT IN THE UNITED STATES

TO obtain information about the economic resources allocated to research and development activities, the National Science Foundation of America has been conducting comprehensive surveys of research and development in the economy on a periodic basis. Such surveys yield economic data that assist the National Science Foundation, the Federal Government, and other public and private organizations to assess the present research and development efforts and to formulate science programmes for the future.

A report* summarizes the results of the 1958 survey of industrial research and development, the survey representing a continuation of the Founda-

* National Science Foundation, Washington. Surveys of Science Resources Series, NSF 61-32: Funds for Research and Development in Industry, 1958. Pp. xvi+119. (Washington, D.C.: Government Printing Office, 1961.) 65 cents.

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tion's series of annual surveys of research and development in industry that began in 1953.

Funds for research and development performance in the industrial sector of the economy totalled 8·2 billion dollars in 1958. More than half this total was for research and development performed in the aircraft and parts, electrical equipment and communication industries, which were heavily engaged in Federally financed research and development.

The amount spent on industrial research and development in 1958 was 7 per cent higher than the 7·7 billion dollars total for 1957. Increases occurred between 1957 and 1958 in all industries for which separate data were obtained except aircraft and parts and rubber products. The relative increase in research and development of companies with less than 5,000 employees (15 per cent) exceeded that of companies with 5,000 or more employees (6 per cent) between 1957 and 1958.

More than half (56 per cent) the industrial research and development performance was financed by the Federal Government. Industries with the highest proportions of federally financed research and development performance were aircraft and parts (85 per cent) and electrical equipment and communications (68 per cent).

In contrast to the large Federal research and development financing in certain industries, 90 per cent or more of the total funds for research and development performance were from company funds in the following industries: food and kindred products, paper and allied products; drugs and medicines; other chemicals; stone, clay and glass products; primary ferrous products; and petroleum refining and extraction. The chemical and allied products industry exceeded all others in the dollar volume of company-financed research and development.

Companies with 5,000 or more employees accounted for 84 per cent of the funds for performance of industrial research and development, compared with 7 per cent in companies with less than 1,000 employees and 9 per cent in companies with 1,000–4,999 workers.

An estimated number of 11,800 industrial firms carried out research and development in 1958, including 10,300 manufacturing companies and 1,500 non-manufacturing companies. In terms of research and development moneys, however, manufacturing companies accounted for 98 per cent of the total. Funds for research and development in 1958 were distributed by the character of work as follows: basic research, 4 per cent; applied research, 23 per cent and development, 73 per cent. Approximately three-fifths of the 295 million dollars for basic research was expended in the physical and mathematical sciences, about one-fifth in the engineering sciences, and the remainder in the life and other sciences.

The product fields of guided missiles, communication equipment, and aircraft and parts accounted for more than half the 7·9 billion dollars utilized for applied research and development. Although the companies in the aircraft and parts, and electrical equipment and communication industries accounted for most of this, companies in other industries also performed substantial amounts of applied research and development in these product fields.

The dollar volume of research and development performance per research and development scientist and engineer in 1958 was 32,900 dollars for all industries combined. Among major industry groups the average ranged from 16,400 dollars in food and kindred products to 52,500 dollars in motor vehicles and other transportation equipment.

Funds for industrial research and development comprised 3·8 per cent of net sales in manufacturing companies performing research and development. Total performance includes federally financed research and development, which amounted to 56 per cent of the total amount for 1958. Research and development performance funds as percentages of net sales were highest in the following separately reported industries: aircraft and parts (17·7 per cent), electrical equipment and communication (10·5 per cent), and scientific and mechanical measuring instruments (9·9 per cent).

STRUCTURE OF ALPHA-KERATIN

By Prof. S. KRIMM

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THE structure of α-keratin[1] has been assumed to be based on the α-helix[2] following the demonstration[3,4] that the coiling of such helices, possibly arising from periodic axial distortions[5,6], can account for the presence of the 5·15 Å. and 1·5 Å. meridian reflexions in the X-ray diffraction pattern. In particular, a three-stranded rope[6] seemed to account satisfactorily for the main features of the diffraction pattern[3,4]. Recent work[7], however, indicates that this structure may not be entirely satisfactory in explaining the details of the pattern, and other models involving additional layers of helices have been suggested[8]. The present ideas do not satisfactorily account for the changes in the X-ray pattern resulting from treatment with heavy metals[9,10], nor for some of the longitudinal regularities found in the matrix component of α-keratin by electron microscopy[10].

It is the purpose of this article to explore a possibility which has not been considered before and which seems to have merit in accounting for much of the data. Specifically, it is proposed that in the two-phase structure of α-keratin consisting of microfibrils and matrix; the latter, far from being amorphous or disorganized, consists of a relatively highly organized structure. In particular, whereas the microfibrils, as is known, compose the α-helical component, it is suggested that the matrix is built up of a structure similar to that of feather keratin, and that this matrix structure accounts for the 198 Å. fibre period[11,12] and the various orders of it which are observed and which are intensified by heavy-metal treatment.

In considering the evidence which suggests this proposal, it may first be noted that the characteristic α-keratin spacings at 5·15 Å. and 1·5 Å. may not, and indeed need not, be correlated with the 198 Å. repeat. Although accurate diffractometer measurements[13,14] give the former spacing as 5·18 Å., which would be a reasonable 38th order of 197 Å., it is not

required that this be true in order to account for this spacing. Secondly, the many orders of 198 Å. which can be observed[11] bear a striking resemblance to the orders of the 189 Å. repeat observed in the diffraction pattern of feather keratin[15], a fibrous protein which contains no α-helix component. Thirdly, the uptake of metals occurs primarily in the matrix, which is rich in cystine compared to the microfibrils[16]. Since this treatment affects primarily the low orders of the 198 Å. meridional repeat[10] (the effect on the low-angle equatorial spots is also accounted for by penetration of the matrix by the reagent[9]), it is not unreasonable to suppose that the component giving rise to this long repeat is distinct from the α-helical component located in the microfibrils.

The correlation of the matrix component of α-keratin with a feather keratin type of structure is suggested by the results of recent work on the structure of the latter fibrous protein[15,17]. These investigations indicate that a structure which is in reasonably good agreement with the data can be developed from the hypothesis that proline residues are distributed periodically along an essentially extended polypeptide chain. Amino-acid analyses, and the presence of a strong 8th order of the 189 Å. fibre axis repeat, are consistent with the proposal that in feather every 8th amino-acid along the chain is proline[17]. The 198 Å. fibre axis repeat of α-keratin (which although slightly larger than that of feather keratin is nevertheless consistent with similar values found for other proteins giving the feather keratin pattern; cf. 197·5 Å. for *Varanus* claw[18]) also is characterized by a strong 8th order reflexion[12]. Chemical analyses[19–21] have indicated that the matrix component of high cystine content is that which is high in proline. The proline content found[21] is of the same order as that found in feather[23], and at the present state of the analysis it can be said that they could indeed be equal. The chemical composition therefore is entirely consistent with the presence in the matrix of the proposed type of extended chain structure. It should be noted that infra-red spectra of α-keratins indicate the presence of a β-component oriented with respect to the fibre axis[23,24].

If we accept this possibility, then we find further that the proposed feather keratin structure[17] can account for several other of the dimensional features of α-keratin. Thus, the predominantly observed fibre axis repeat in feather is expected to be half of 189 Å. (ref. 17), and this fits in well with the approximate 95 Å. longitudinal periodicity seen in electron micrographs of the matrix of α-keratin[10]. Again, the diameter of the predicted fibrillar unit for feather keratin is about 22 Å. (ref. 17). Electron micrographs of wool[16] show that in the paracortex there are microfibrils of diameter about 60 Å. the centre to centre separation of which is about 83 Å. These dimensions are consistent with each microfibril being separated from its neighbour (in an essentially hexagonal array) by one feather keratin unit. Twelve feather keratin units will just pack around one microfibril. Finally, the observation[25] that hydration of dry α-keratin results in preferential swelling of the matrix in comparison with the microfibrils may be understandable in terms of the open type of structure suggested for feather keratin[17].

The above proposal of two structural components in α-keratin can also help to explain the results of heavy-metal treatments. Recent investigations of this kind[26] suggest that cystine is periodically located along the polypeptide chain of feather keratin (with a periodicity of about 47·3 Å.). The same may be true for α-keratin. Amino-acid analyses[21] show that the matrix of α-keratin has about twice as much cystine as does feather. If these residues were periodically located along the chain, we would expect heavy-metal treatment to enhance in all cases the 8th order of the 198-Å. fibre axis repeat. This is precisely what is found[9,10]. This evidence itself suggests that the matrix component of α-keratin may be a relatively highly organized structure.

There is another important characteristic of α-keratin which could be accounted for by the proposed model. Recent work on the α → β transformation in keratin[27–29] has indicated the complex nature of this process and the likelihood that a simple transformation of a single chain from α-helix to β-extended chain is not involved. Suggestions have been made that the transformation may proceed through an intermediate phase[27,28], or that there may be two crystalline phases[29,30]. The foregoing model would fit in with the latter scheme, extension of the microfibrils leading to loss of the α pattern whereas further extension of the (already nearly extended) matrix component would result in the development of the β pattern. The detailed mechanics of this process (which may, for example, involve the relative sliding of the two components with respect to each other) perhaps cannot be specified at this point, but the general mechanism does not seem to be eliminated by the available data.

In summary, it is suggested that the matrix component of the two-phase structure of α-keratin consists of a relatively ordered polypeptide chain structure basically similar to that of feather keratin, and with which is associated the long axial periodicities in the X-ray diffraction pattern.

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CRYSTAL STRUCTURES OF SALTS OF METHYLATED PURINES AND PYRIMIDINES

By R. F. BRYAN and K. TOMITA

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NUMEROUS patterns of hydrogen bonding have been postulated between purines and pyrimidines in the various models which have been proposed for the structures of nucleic acids and their synthetic analogues. It is a disadvantage of the method of fibre crystallography, which is most directly applicable to the study of such structures, that it does not allow a refinement of the structural parameters based solely on the diffraction data, and hence it is important that structures proposed to explain fibre diffraction diagrams should be both chemically and stereochemically acceptable as well as in reasonable agreement with the diffraction evidence[1]. An examination, by X-ray diffraction techniques, of single crystals of salts of methylated purines and pyrimidines (the simplest analogues of nucleotides) might be expected to yield three valuable pieces of information which would be of use in the formulation of structures for nucleic acids; first, a knowledge of the molecular geometry of the various bases; secondly, an identification of the sites of protonation of the bases at acid *p*H; thirdly, a possible model for the geometry of inter-base hydrogen bonding in polynucleotides. With this in mind, we are conducting a systematic survey of acid salts of such methylated purines and pyrimidines and wish to report some of the results of work on two of these, 9-methyladenine dihydrobromide and 1-methylcytosine hydrobromide.

Crystals of 9-methyladenine 2-hydrogen bromide are orthorhombic with $a = 17{\cdot}59 \pm 0{\cdot}05$ Å., $b = 4{\cdot}88 \pm 0{\cdot}02$ Å., and $c = 11{\cdot}75 \pm 0{\cdot}04$ Å. The space group is $Pna2_1$ with four molecules of the dihydrobromide in the unit cell. The crystal structure was determined, using the heavy atom method, from examination of the (010) and (001) projections and refined, using Fourier and difference Fourier syntheses. In addition, the (*h*0*l*) data were further refined by least squares methods. Fig. 1 shows the electron density distribution $\rho(x,z)$. Each molecule of methyladenine is enclosed by a three-dimensional network of Br^- ions, the Br . . . Br contacts ranging in length from 4·25 to 5·17 Å.

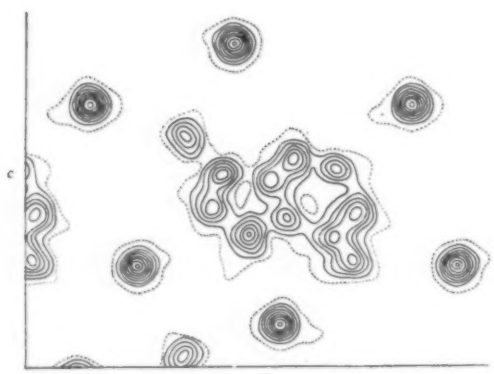

Fig. 1. Electron density $\rho(x,z)$ for 9-methyladenine 2-hydrogen bromide. Contours at equal but arbitrary intervals, intervals for Br^- × 5

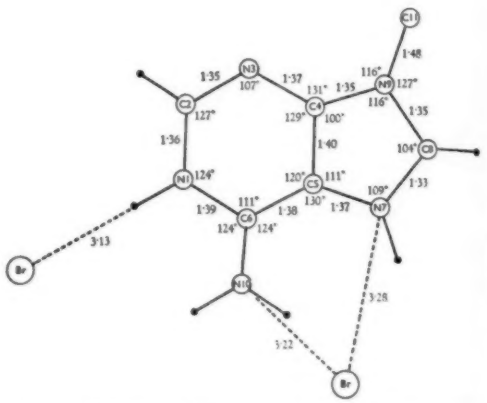

Fig. 2. Interatomic distances and angles for 9-methyladenine 2-hydrogen bromide

The conventional residuals, *R*, excluding unobserved reflexions, are 0·07 for (*h*0*l*) and 0·11 for (*hk*0). Despite these low values the overall accuracy of the structure determination is only fair, the standard deviation in the position ascribed to carbon or nitrogen atoms being about 0·05 Å., and the good agreement between observed and calculated structure factors may be attributed mainly to the very accurate location of the two bromine ions. The details of the molecular geometry are shown in Fig. 2. Although the dimensions found for the cation of 9-methyladenine are reasonable, no useful comparison can be made between them and the dimensions found by Cochran[2] for the adenine molecule in adenine hydrochloride, nor with those proposed by Pauling[3] or by Spencer[4] for the adenine molecule as it is assumed to exist in nucleic acids. This illustrates the disadvantage of using compounds containing such heavy atoms where particularly accurate molecular dimensions are sought. From our point of view, however, the most interesting feature of the structure is the hydrogen bonding pattern. There are no hydrogen bonds joining the purine molecules directly, each molecule forming instead three hydrogen bonds to neighbouring Br^- ions. This is most probably because access to the only remaining acceptor atom on the adenine molecule, N(3), is hindered by the 9-methyl group. It is likely, indeed, that because of a similar effect exercised by the sugar molecules, no structures involving N(3) as an acceptor atom in hydrogen bond formation can occur in multi-stranded polynucleotide structures. The hydrogen bonds which

are formed are: N(1)—H . . . Br(1), 3·13 Å.; N(10)—H . . . Br(2), 3·21 Å.; and N(7)—H . . . Br(2), 3·28 Å. All these bonds are shorter than the more usual length found, 3·4 Å., at least two of them by significant amounts, and we postulate a strong electrostatic contribution to the bond energies. All other intermolecular contacts are of normal lengths.

The fact that the protonated nitrogen atoms are N(1) and N(7) provides additional evidence for the correctness of the structure proposed by Rich, Davies, Crick and Watson[1] for polyadenylic acid. Fibres of this substance show poor orientation at neutral *p*H, but a high degree of orientation when the *p*H is lowered somewhat. At still lower *p*H, however, the orientation again disappears, though the molecular weight remains unchanged. Following Cochran[2], Rich *et al.* assume protonation of the adenine at N(1) with a consequent internal neutralization of the overall charge of the molecule. The two strands of the helical molecule are assumed to be held together by pairs of hydrogen bonds between the 6-amino group and N(7). The disappearance of orientation at the very low *p*H can thus readily be explained as due to the disruption of this hydrogen bonding consequent on protonation of N(7).

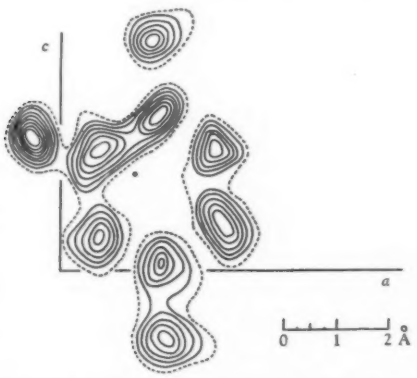

Fig. 3. Electron density $\rho(x,z)$ for 1-methylcytosine hydrogen bromide. The contribution of the Br^- ion has been subtracted from the structure factors; its position is indicated by the dot

1-Methylcytosine hydrogen bromide also occurs as orthorhombic crystals with $a = 12{\cdot}98 \pm 0{\cdot}03$ Å., $b = 6{\cdot}80 \pm 0{\cdot}02$ Å., and $c = 8{\cdot}83 \pm 0{\cdot}02$ Å. The space group is *Pnma* with four molecules in the unit cell which, in consequence, occupy the mirror planes of symmetry at $y = \frac{1}{4}$ and $\frac{3}{4}$. The structure was solved from the (010) projection by making use of the heavy-atom method. The molecular arrangement is somewhat unusual and this caused us some initial difficulty in deciding on a correct trial structure. In projection, a Br^- ion at $y = \frac{1}{4}$ is situated roughly in the centre of a cytosine ring at $y = \frac{3}{4}$. Fig. 3 shows a synthesis of the type $(F_o - F_{Br})$ giving the electron density $\rho(x,z)$ with the contribution of the Br^- ion removed. This sandwiching of the bromine ions between the heterocyclic rings leads to a very efficient type of interlayer packing. A similar arrangement is found in the case of 9-methylguanine dihydrobromide (work still in progress).

The structure was refined by means of difference Fourier syntheses to a value for the index R of 0·12 for (*h*0*l*). Structure factors were also calculated, as a check, for (*h*1*l*) and (*h*2*l*), giving the same value of

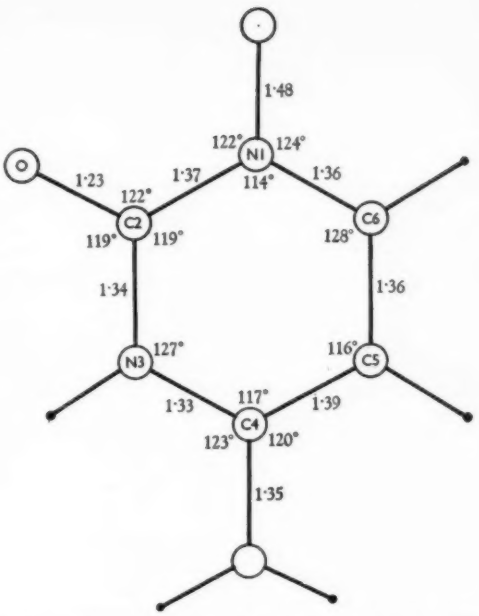

Fig. 4. Bond-lengths and angles in the cation of 1-methylcytosine

R as for (*h*0*l*) in each case. Fig. 4 shows the molecular dimensions found for the cation of 1-methylcytosine. The bond-lengths found (σC—C = 0·03 Å.) are in good agreement with those suggested by Pauling[3] and by Spencer[4] for the cytosine molecule as it is assumed to occur in nucleic acids. The sum of the individual differences in bond-lengths between our dimensions and those of Pauling is 0·10 Å., and for the Spencer model this sum is 0·08 Å. However, some of the bond-angles which we find are in marked disagreement with those suggested by either Pauling or Spencer. The average difference is 6°; the maximum difference is 10°. We estimate[5] our standard deviation in bond-angle to be about 2°, and so these differences would seem to be significant in some cases.

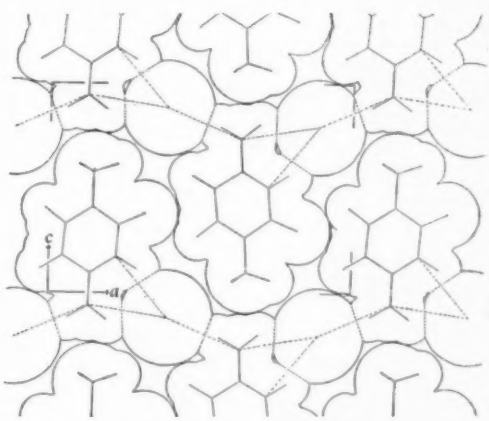

Fig. 5. Packing drawing of the arrangement of molecules within a layer of the structure of 1-methylcytosine hydrogen bromide. Conventional van der Waals radii are inscribed; hydrogen bonds are indicated by the lines

However, owing to the overlap, in projection, between the Br^- ion and the cytosine ring it is possible that the errors in the positions of some of the atoms in our structure are in excess of our estimate which is based on the assumption of non-overlapping atoms. We are therefore not prepared to offer our values for these angles as being intrinsically better than those in either of the two models with which we compare them. A subsequent three-dimensional refinement may enable us to improve the accuracy of this determination.

The cytosine ring is protonated at N(3) and there are again no hydrogen bonds between individual base molecules. Instead, each ring forms three hydrogen bonds of length 3·36, 3·39 and 3·40 Å. to adjacent Br^- ions as illustrated in Fig. 5, which also shows the molecular packing within a given layer. Since the molecules are planar it is possible to inscribe the conventional van der Waals radii of the atoms, and this has been done in Fig. 5. It is seen that the packing is extremely efficient with the molecules forming an interlocking double dovetail arrangement, the backbone of the individual dovetail units being the hydrogen bonds. Particularly noteworthy is the manner in which the Br^- ion lies between N(3) and the 4-amino group and thus takes part in two hydrogen bonds. The deviation from linearity in each of these bonds is in excess of 25° and illustrates the large distortions which can be tolerated in such bonds where there is a compensating electrostatic interaction.

This work was supported by grants from the National Cancer Institute of the U.S. Public Health Service and the American Cancer Society. One of us (R. F. B.) was in receipt of a U.S. Public Health Service postdoctoral fellowship.

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INTERACTION OF LIGHT AND ATMOSPHERIC PHOTOCHEMICAL PRODUCTS ('SMOG') WITHIN PLANTS

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DAMAGE to plants from ozone and peroxyacetyl nitrate, two photochemically formed components of 'smog', has been described[1–3]. However, variations in symptom expression and the degree of damage caused by a given concentration of these components, whether of synthetic or natural origin, have complicated development of an adequate biological assay method for these materials. These observed variations in symptomatology have implicated stomatal action, inorganic nutrition, temperature, genetics, ascorbic acid content, physiological age of tissue and photoperiod[4–8]. Plants grown under artificial illumination differ in their response to the photochemically formed pollutants as compared with plants grown in the greenhouse. Interactions between light and oxidants from the polluted atmosphere within plants, as reported here, might well explain some of the variabilities in symptomatology observed in earlier controlled experiments as well as the unexplained natural variability observed in the Los Angeles area. The results presented also emphasize the importance of standardizing plant growth conditions for future work of this nature.

Lots of pinto bean (*Phaseolus vulgaris*) and petunia (*Petunia hydrida*, var. Rosy Morn) plants were grown under the following light conditions: (1) natural light received in the greenhouse during August–November; (2) a 15-hr. photoperiod of 8·6 Klux from cool white fluorescent lamps in a shaded greenhouse and (3) a 15-hr. photoperiod of 21·5 Klux from Sylvania 'very high output (VHO)' fluorescent lamps also in the shaded greenhouse. Approximately 85° F. day and 70° F. night temperatures were maintained. Plants were exposed to the oxidants in chambers placed under a 21·5 Klux fluorescent lamp panel. Dark chambers in the greenhouse were used for the experimental dark conditions. The greenhouses and fumigation chambers were supplied with carbon-filtered air[9] to remove the naturally occurring oxidants.

To ensure that the stomates were open at the time of exposure to the oxidants, all plants pre-conditioned by a dark period were given 15–30 min. light before exposure to the oxidants. Stomatal opening was determined by a resistance porometer[10] with a leaf-cup attached to a snap spring device to ensure a rapid seal to the leaf. In later experiments the porometer measurements were supplemented with transpiration measurements. During the 15–20 min. before exposing the plants to the oxidants the rate of water-loss by transpiration was followed. When this rate of water-loss equalled the rate of water-loss from the pre-light treated plants the fumigation was started.

Plants were exposed to the oxidants for periods of 30 min. or less. After exposure, unless otherwise specified, the plants were returned to the pre-treatment light condition. Symptoms of oxidant damage were usually apparent within 4 hr.; however, assay of damage was made 48 hr. after exposure to the oxidants. The extent of damage was expressed as the percentage of leaf area showing symptoms of the oxidant injury. Eight to twelve plants were used in each treatment and the experiments were repeated several times.

The type and extent of ozone and peroxyacetyl nitrate injury on bean and petunia plants were affected by light intensity under which the plants were grown before treatment. Sensitivity to ozone injury was increased by the low light intensity (8·5 Klux), while sensitivity to peroxyacetyl nitrate was increased by the higher light intensity (21·5 Klux). A total bleaching and collapse of affected leaf tissue characterized the oxidant injury on plants grown under the

low light intensity. By contrast, oxidant injury on plants grown in the higher light intensity usually appeared as bronzing of the lower leaf surface, and ozone injury on the bean appeared as discrete dark brown spots on the upper leaf surface.

Sensitivity of pinto bean and petunia plants to peroxyacetyl nitrate was significantly affected by the presence of light immediately before, during or after exposure to the toxicants. A 24-hr. pre-treatment dark period completely protected these plants against peroxyacetyl nitrate damage (Fig. 1 *DL*) regardless of subsequent light régime during and after fumigation. Plants which had received the standard 15-hr. day, with a 5- to 6-hr. light period immediately preceding the fumigation, were severely damaged (Fig. 1, *L*), whereas similar plants transferred to the dark for 24 hr. after fumigation were uninjured (Fig. 1, *LD*). Bean plants returned to the light after the 24-hr. post-dark period appeared normal and did not develop oxidant damage, whereas some oxidant damage did develop on the petunia plants after transfer to the light.

In another series of experiments, bean plants were fumigated with very high concentrations (5 p.p.m.) of peroxyacetyl nitrate for 10 min. All the plants were grown under the 15-hr. light régime and were returned to the lights after the 10-min. fumigation. Darkness during this short fumigation period gave complete protection from damage to petunia and bean plants while identical plants fumigated similarly in the light were severely damaged (Fig. 2). Porometer measurements showed that during the 10-min. dark period the resistance to air-flow through the stomates decreased only 0·028 unit[10], an insignificant change. This indicated that the observed results were related to the interaction of light and some product in the plant and not to the exclusion of peroxyacetyl nitrate by closed stomates.

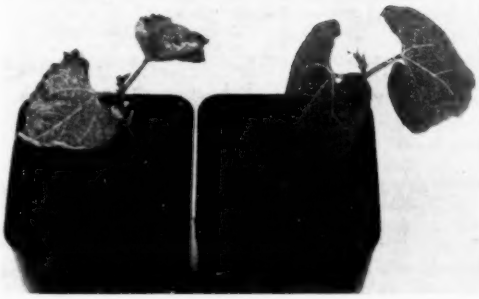

Fig. 2. Ten-day-old pinto bean plants exposed to 5 p.p.m. peroxyacetyl nitrate for 10 min. Left, light before, during and after fumigation—severe damage. Right, light before, dark during (10 min.) and light after fumigation—undamaged

Fig. 1. Pinto bean plants fumigated for 30 min. with 1·0 p.p.m. of peroxyacetyl nitrate
DL, dark before (24 hr.), light during and after fumigation—no damage; *L*, light before (6 hr.), during and after fumigation—severe damage; *LD*, light before and during fumigation and dark (24 hr.) after fumigation—no damage

The interaction of light and ozone was unlike that of light and peroxyacetyl nitrate. A considerably longer pre-treatment of dark period (48 hr. or longer) was necessary to provide protection to petunia and bean plants from an ozone fumigation (Table 1). The marked reduction in extent of ozone damage that occurred as the pretreatment dark period was lengthened beyond 24 hr. suggests that susceptibility may be dependent on the level of photosynthate or some carbohydrate intermediate within the tissue. Further evidence of the difference in action of peroxyacetyl nitrate and ozone was shown by the damage response obtained with a short, dark period during fumigation and with 24-hr. post-dark treatment. Both these conditions prevent oxidant injury from peroxyacetyl nitrate but have no effect on ozone damage. There were indications from additional experiments that under the conditions of these experiments the bean required at least 3–4 hr. of light after fumigation for symptoms of damage by peroxyacetyl nitrate to develop.

The distinct interrelationship of light with the oxidizing air pollutants in plants definitely shows that there is a photochemical reaction between the oxidant and some intermediate synthesized by light in the plant. The reactions of this intermediate with the oxidant peroxyacetyl nitrate is further dependent on light to cause a change in the metabolism of the plant sufficient to induce irreversible leaf damage.

Table 1. Effect of Varied Lengths of Dark Treatments Before, During and After Fumigation on the Percentage of Pinto Bean Leaf Area Injured by Ozone and Peroxyacetyl Nitrate (PAN)

Fumigant and concentration	Pre-dark period (hr.)*	Condition during fumigation	Condition after fumigation	Injury (per cent)†
Ozone, 0·6 p.p.m.	0	light	light	76
	24	,,	,,	77
	48	,,	,,	0
	0	,,	dark	80
PAN, 1·0 p.p.m.	0	,,	light	99
	24	,,	,,	0
	48	,,	,,	0
	0	,,	dark	0

* The pre-dark period started at 9 a.m. The plants were grown under fluorescent lamps of 21·5 Klux with a light period of 15 hr. (4.30 a.m.–7.30 p.m.). The plants were moved into the light at 9 a.m. and fumigation started after the stomates had opened (15–30 min.). A resistance porometer was used to determine when the stomates were open.

† Average values from 8–12 plants per treatment.

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ACID-SOLUBLE NUCLEOTIDES OF *STAPHYLOCOCCUS AUREUS*: MASSIVE ACCUMULATION OF A DERIVATIVE OF CYTIDINE DIPHOSPHATE IN THE PRESENCE OF PENICILLIN

By Dr. J. J. SAUKKONEN
Biochemistry Laboratory, State Serum Institute, Helsinki

PENICILLIN is known to cause accumulation of three uridine nucleotides in *S. aureus*[1]. The compounds were identified by Park as uridine diphosphate (UDP)–acetylmuramic acid, its alanine derivative, and a nucleotide composed of a peptide (ala-glu-lys-ala-ala) and UDP–acetylmuramic acid[2]. Several aspects of nucleotide accumulation in the presence of penicillin or other anti-bacterial substances have been investigated extensively[3]. On the basis of their findings, Park and Strominger have suggested that penicillin might be a specific inhibitor of transfer of the peptide from the most complex of the above nucleotides to the cell wall structure[4]. Relatively little attention has been paid to other nucleotides present in penicillin-treated cells. Strominger has investigated the acid-soluble extract of penicillin-inhibited *S. aureus* by means of anion exchange chromatography[5]. In addition to the UDP-derivatives, cytidine-5′-monophosphate (CMP), adenosine-5′-monophosphate (AMP) and small amounts of unidentified ultra-violet-absorbing substances were detected. Penicillin was reported to cause a doubling in the amount of CMP, when compared with untreated cells. Park and Strominger have noted, according to a personal communication to Armstrong *et al.*[6], the accumulation of cytidine diphosphate (CDP)–ribitol in *S. aureus* during treatment with penicillin and crystal violet. A report of the accumulation of this nucleotide induced by crystal violet has been published[7]. In the course of another investigation, indications were found of the presence of a large number of nucleotides in *S. aureus*, prompting the present work.

S. aureus 209 Pfeiffer (obtained from Dr. I. Rantasalo of this Institute) was grown in a medium adapted from that of Park and Johnson[1], with shaking at 37° C. At approximately half maximal growth, penicillin (benzylpenicillin, the Distillers Co., Ltd., London) was added to a final concentration of 10 μgm./ml. culture medium. After incubation for 1 hr., the cells were gathered rapidly in a refrigerated centrifuge and frozen. The pellet was extracted with cold 0·6 *N* perchloric acid and the acid-soluble fraction was neutralized and chromatographed on a 'Dowex-2' column at 4° C., using the gradient elution system of Hurlbert *et al.*[8]. Details of the procedure have been described in ref. 9.

Typical elution diagrams of normally grown and penicillin-treated cells are presented in Fig. 1. In both cases, a number of ultra-violet-absorbing compounds can be detected. Fraction *A*, which represents a large portion of the total ultra-violet-absorbing material, contains several substances. Chromatography of this fraction in a system with better resolution revealed in addition to diphosphopyridine nucleotide and CMP a third major compound in the penicillin-treated bacteria. This compound appears to be a nucleotide giving a positive ninhydrin reaction. Fraction *B* was identified as AMP. Analysis of peak *C*, characterized by its high 275/260-ratio, will be given here. Derivatives of adenine, guanine, uracil and cytosine have been found in the subsequent fractions. Peaks *D* and *E* were shown to be uridine nucleotides containing amino-acids, and presumably correspond to the known derivatives of UDP (ref. 3).

When the two patterns of nucleotides are compared, a striking increase in the amount of fraction *C* is seen in the penicillin-treated cells. Material corresponding to this fraction was collected from several preparations and purified by means of paper chromatography in neutral ethanol – ammonium acetate – water[10]. The small amount of the compound recovered from repeated runs in this system was subjected to further analysis. The substance was found to be uniform in several other solvent systems. The mobilities were close to the values reported earlier[7,11] for CDP–ribitol (in propanol–ammonia–water: R_P 0·36, in neutral ethanol–ammonium acetate–water: R_{UMP} 1·23. The base, which was isolated by means of paper chromatography after vigorous acid hydrolysis[12], gave a typical spectrum of cytosine in 0·01 *N* hydrochloric acid and in 0·01 *N* sodium hydroxide. A colorimetric assay[13] yielded 1·88 moles of phosphorus/mole cytosine. Paper chromatography in propanol – ammonia – water[14] after acid hydrolysis yielded in addition to CMP and inorganic phosphorus other breakdown products, two of which gave a positive reaction for phosphoric esters[14] and with ammoniacal silver nitrate[15]. While it has not yet been possible to identify the phosphoric ester moiety with certainty, the evidence available suggests the compound to be identical with CDP-ribitol[11,16].

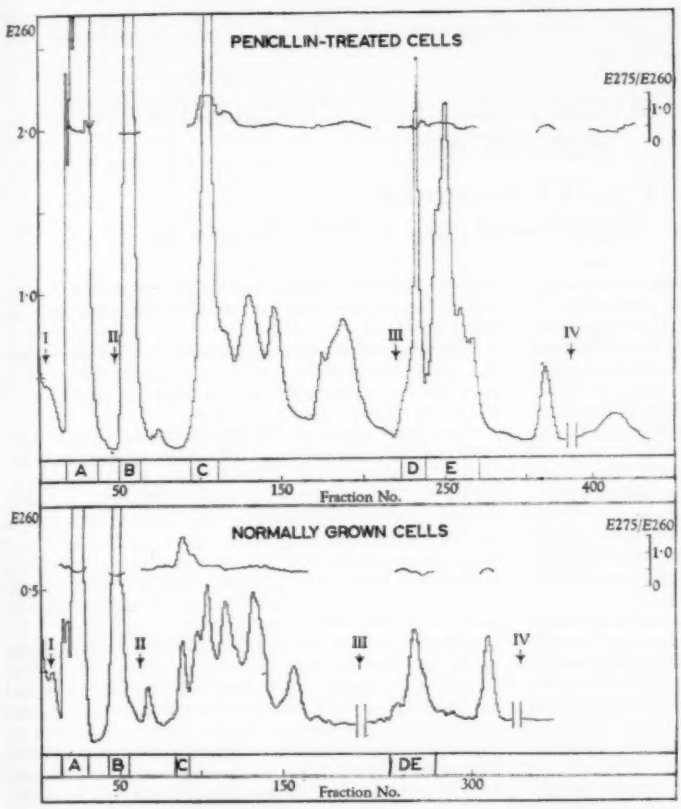

Fig. 1. Anion exchange chromatograms of extracts from penicillin-treated *S. aureus* and from normally grown cells. Bacteria from 4 l. of culture were extracted in both cases. The column was 'Dowex-2', $HCOO^-$, 200–400 mesh, 8 per cent cross-linked. A 1·0 × 18 cm. column was used in the first case, a 1·2 × 15 cm. column in the latter instance. The volumes of the mixing flasks were 450 and 375 ml., respectively. After washing with distilled water, the column was eluted with the following solutions in the reservoir: I, 0·5 *N* formic acid; II, 4 *N* formic acid; III, 4 *N* formic acid and 0·4 *N* ammonium formate; and IV, 4 *N* formic acid and 0·8 *N* ammonium formate, as indicated on the diagrams

The present work shows that a large number of nucleotides is found both in penicillin-treated and in normally grown *S. aureus*, apparently forming a pattern similar to the distribution discovered in some other micro-organisms and in many animal tissues (cf. refs. 9 and 17). The various uridine nucleotides from the extracts of penicillin-treated bacteria have not yet been identified. It is assumed that they belong to the group of UDP-derivatives involved in cell wall synthesis. Ito *et al.* have reported that the UDP-acetylmuramic acid peptides of this strain contain aspartic acid and glycine[18]. The accumulation of uridine nucleotides is paralleled by the massive accumulation of the CDP-derivative, which in many cases surpasses the increase in the amount of individual uridine nucleotides.

The difference between the present results and earlier findings could be due to a number of factors. As pointed out by Strominger in the case of bacteria treated with crystal violet, the accumulation of CDP-ribitol cannot be demonstrated with all strains of *S. aureus*[7]. Possible differences in the composition of the culture medium and in other experimental conditions could also have influenced the results. Baddiley and Mathias, who originally discovered CDP-ribitol and CDP-glycerol in *L. arabinosus*[19], found the compounds very labile during extraction. This was attributed to the presence of potent phosphatases. For this reason, heat-killed bacteria have been used for later investigations. Strominger, who inactivated the enzymes by heating a washed bacterial suspension at 100° C. for 10 min., found great variations in the amount of CDP-ribitol from crystal-violet-treated cells, accompanied by a corresponding change in the amount of CMP (ref. 7). In the work described here, the bacteria were grown in small batches, chilled rapidly and extracted at low temperature. Even a small delay in chilling was found to reduce the amount of the nucleotide considerably. With proper care, this method seems to give high yields of the nucleotide.

It has been suggested that CDP-ribitol might be a precursor of teichoic acid, a component of bacterial cell wall containing ribitol phosphate[6]. While the biology of the accumulation of CDP-ribitol is not well known, it is interesting to note that both penicillin and crystal violet cause accumulation of this nucleotide. These two agents appear to interfere at different points with the uridine nucleotide pathway leading to cell wall synthesis[7]. Whether the accumulation of CDP-ribitol is a result of an independent action of penicillin on the cytidine nucleotide metabolism or whether the accumulation of the two types of nucleotides is caused by an interference with a single reaction in the metabolic sequence, cannot yet be decided.

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SENSORY DEPRIVATION AND FŒTAL CIRCULATORY HOMEOSTASIS

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EMBRYOLOGISTS seem to overlook the effect of a flotation-type of existence *in utero* on physiological activities within a fœtus as compared with physiological capabilities once development has proceeded through the period of morphogenesis. Morphological differentiation must precede functional capability. This is true of single-organ systems or of two or more interdependent systems such as homeostatic regulatory mechanisms. However, full function of one or more completely developed secondary organ systems may not occur because a primary organ system essential to the secondary one is not yet called into action by the exigencies of the environment. It is this sort of system–system interaction that appears to be involved in the circulatory adjustments of the fœtus (lamb) *in utero*.

The problems of fœtal heart-rate, blood pressure and reflex mechanisms have been reviewed by Windle[1] and Barcroft[2]. In 1954, when fœtal blood pressure and heart-rate were recorded *in utero* with the membranes intact[3], fœtal circulatory characteristics could be studied in nearly normal circumstances. In such a preparation, responses to a variety of stressful situations were determined.

Parasympathetic and sympathetic nervous system capabilities were explored, largely with the fœtus *in utero*. Included were the responses of heart-rate and blood pressure to: (*a*) increased intrauterine pressure[4]; (*b*) graded degrees of hypoxia[5]; (*c*) disturbances of the maternal circulation[6]; (*d*) occlusion of the umbilical cord[7]; (*e*) vagotomy[8]; (*f*) stellate and thoracic ganglionectomy[8]; (*g*) excision of the fœtal adrenal glands[9].

The resting fœtal heart-rate decreases when intrauterine pressure increases by a weight placed on the uterus and decreases when the weight is removed. These are transient episodes evoked by a brief and dynamic stimulus. The bradycardia is vagal in origin since it is abolished by atropine. There is, therefore, a competent vagal mechanism which is brought into temporary action by this change in the environment.

A lamb *in utero* and its mother respond differently to the same asphyxial stimulus. When nitrogen is given to a ewe, her heart-rate and blood pressure rise. The fœtus shows bradycardia and no change in blood pressure. When atropine is given to the fœtus during bradycardia the heart-rate becomes rapid. The bradycardia is vagally induced. Again we see that the autonomic system of the lamb responds to this stress by parasympathetic output and the fœtal response is unlike that of the adult.

Less stressful stimuli have an effect also. When a pregnant ewe is subjected to progressively stronger hypoxia, the fœtal heart-rate decreases or it shows a 2 : 1 heart block which is vagal in origin. Similarly, if there are acute disturbances of the maternal circulation involving transient congestion of the maternal portion of the placenta, evanescent decreases in fœtal heart-rate occur. This is the result of induced vagotonia.

From these and other experiments we conclude that the parasympathetic system of the fœtal lamb is functionally competent, but it lacks a stimulus to maintain parasympathetic tone.

Most of the present observations were made with ewes lightly anæsthetized with diallylethylabarbituric acid. It might be argued that this anæsthetic abolishes existing vagal tone. This is unlikely, however, since vagotonia is the easiest response in the lamb to exhibit under this anæsthesia and experiments made with the ewe operated under local anæsthesia ('Procaine') alone make no difference in the fœtal responses to stress or in the resting characteristics of the fœtal circulation.

Barcroft found progressive vagotonia as a fœtal lamb becomes larger. However, the *in utero* rates observed by him were recorded by auscultation and by palpation which involved some pressure on and handling of the uterus which, as we have shown, induces vagotonia. From Barcroft's experiments on lambs at Cæsarean section, it appears that the acute response to stress of handling induces vagotonia, since he operated and observed very rapidly. He says, "Let me emphasize again, that if the phenomena which have just been described [fœtal vagotonia] are to be observed they must be observed at once on the delivery of the fœtus—a delivery which must be carried through with no strain on the uterine and umbilical blood vessels and no exposure of the cord or fœtus—it may seem wasteful to do an experiment on a sheep which only takes 10 min. and produces but a single lesion, but it is less wasteful than for him to misinform himself on 3 or 4 matters" (ref. 2, p. 137).

Concerning sympathetic activity in the fœtus, evidence is meagre but equally clear. When normal resting fœtal heart-rates in lambs are compared with resting heart-rates after bilateral excision of the stellate and other thoracic sympathetic ganglia, no change occurs in resting fœtal heart-rate. This is true whether the vagi are intact or sectioned or both carotid sinus areas are excluded from the circulation. One must conclude that there is no appreciable resting sympathetic tone in the fœtus so far as heart-rate is concerned.

One type of evidence has been obtained which resulted in sympathetic system activity in the fœtus. With the heart completely denervated severe anoxia was produced by temporary occlusion of the umbilical cord. The heart-rate showed a slow but profound decrease, due to myocardial depression. On release of the cord, an extremely fast and prolonged tachycardia was seen. The fœtus struggled, exhibited strong expiratory effort and passed meconium. The experiment was repeated after incision of both fœtal adrenal glands. After anoxia, the heart-

rate returned to normal without tachycardia. *In extremis*, therefore, there was mass stimulation of the sympathetic system.

One must conclude that the sympathetic system of the lamb fœtus, like the parasympathetic system, is functionally competent but inactive in a resting fœtus. One asks, therefore, why a developed and competent autonomic system is silent except in the face of transient and dynamic stresses.

Examination of the development of cardiovascular responses in lambs soon after birth is crucial to the hypothesis suggested above. A few observations have been made in lambs 4–12 days of age, averaging about 8 days. Responses to the following stresses have been studied: (*a*) carotid artery occlusion (6 lambs); (*b*) bilateral vagotomy (8 lambs); (*c*) severe hypoxia (9 lambs). The results are summarized in Tables 1, 2 and 3.

Table 1 shows that carotid artery occlusion in lambs yields a rise in blood pressure like that of the adult; the heart-rate response is more or less intermediate between the adult and the fœtus.

Table 1. Comparison of the Effect of Carotid Artery Occlusion in Fœtuses, Lambs and Ewes

	Blood pressure (per cent)*			Heart-rate (per cent)*		
	+	○	−	+	○	−
Non-pregnant ewes (ref. 10)	100	0	0	50	20	30
Lambs (ref. 6)	100	0	0	33	0	67
Fœtuses (ref. 5) (last third preg.)	20	60	20	0	20	80

* Percentage of animals showing increase (+), no change (○) or decrease (−).

Table 2 shows that vagotomy in adult ewes and lambs causes a fall in blood pressure and a decrease in heart-rate while blood pressure in fœtuses is unchanged, although the decrease in heart-rate occurs. The effect of vagotomy in the lamb parallels more closely the change in the adult than in the fœtus.

Table 2. Comparison of the Effects of Vagotomy in Fœtuses, Lambs and Ewes

	Blood pressure (mm. Hg)		Heart-rate (b.p.m.)	
	Before	After	Before	After
Non-pregnant ewes (ref. 12)	101·5 (±8·9)/ 81·8 (±8·2)	87·3 (±8·5)/ 64 (±6·6)	110·4 (±8·5)	99·5 (±6·5)
Lambs (ref. 6) (mean blood pressure)	85	70·5	234	194
Fœtuses (ref. 5) (mean blood pressure)	37·9 (±4·4)	37·8 (±2·4)	166·7 (±13·7)	158·8 (±14·0)

Altbough there is a great variability of response in the effects of severe hypoxia in all three groups, Table 3 shows that the blood pressure of the fœtus was, with one exception, unaffected by acute hypoxia. The responses in lambs and adults are rather similar. The heart-rates were variable, but once again the lambs and ewes resemble each other to the extent that some of each showed cardiac acceleration which was not seen in the fœtus.

These results suggest that new-born lambs resemble adults in their responses to the three stresses employed. More refined experiments are needed to establish this point, but the evidence seems clear that circulatory homeostasis begins soon after birth in the sheep.

Table 3. Comparison of Effects of Hypoxia in Fœtuses, Lambs and Ewes

	Blood pressure (per cent)			Heart-rate (per cent)		
	+	○	−	+	○	−
Ewes (ref. 15)	33·4	46·6	13·4	46	46·6	13·4
Lambs (ref. 9)	55·5	33·4	10·1	33·4	20·2	44·5
Fœtuses (ref. 7) (last trimester)	0	86·7	13·4	0	42·8	57·2

Recent experiments on men given bed rest[9] or immersed in water for a day to a week[10] show that cardiovascular homeostasis depends on proprioceptive input to the central nervous system. Following immersion there is a progressive decline in blood pressure, an increase in heart-rate, and a loss of the diurnal variation in heart-rate. The response of heart-rate to the mild stress of a tilt table was much exaggerated. An elevation of diastolic and a decrease of systolic blood pressure occurred, signifying diminishing cardiac output. With more severe stress of exercise on a treadmill, the deficiency of homeostasis was more exaggerated. In short, prolonged reduction of proprioceptive input by weightlessness leads to loss of effective homeostatic regulation in man and exaggerated sympathetic system output.

The concept that homeostatic regulatory mechanisms depend on sensory input to the nervous system is nicely set forth in a recent book by Stanley-Jones[12] in which the roles of monitoring positive and negative feed-backs in a wide range of biological systems are reviewed. Feed-backs acting on physiological mechanisms result in stabilization; consequently they prevent by negative feed-back a runaway to a maximum (for example, excessive sympathetic activity as in the deconditioned man[10]).

Stanley-Jones distinguishes between two main types of sensory inputs: (1) those in which brief reflex responses occur and are dynamic in the sense that they elicit reflexly a response of limited duration and a purposeful nature, and (2) those that serve to produce a sustained sensory input, activating the nervous system on a long, continuing basis. The former are responses to quickly adapting sense organs, the latter, to slowly adapting sense organs. In the main, the second type have their origin in postural input nervous mechanisms from otoliths and from muscle spindles. Speaking of antigravity feed-back in higher vertebrates he says: "The new feature . . . is the augumentor system. It is Nature's response to the challenge of gravity. It employs a positive refection (feed-back) to maintain the posture of the body when at rest, instead of the negative refection used in fishes. . . . The muscle spindle is the little machine inside the big machine". Speaking of weightless adults deprived of all sensory input, Stanley-Jones says: "The physical status of adults in these circumstances resembles nothing so much as a return to the fœtal condition of isothermal floating in the amniotic fluid of the womb; it is not surprising therefore that the body regression to prenatal conditions should cause a similar regression on the mental plane". With respect to the latter reference, the reader should consult an editorial on the subject[13].

The fœtus *in utero*, like the immersed man in Graveline's experiment, is a free-floating organism. As in that experiment, the fœtus is in a sort of zero-gravity situation so far as weight is concerned. It is not called on to use its proprioceptive reflexes to offset the effect of gravity in order to maintain posture. The fœtus is subject to no unequal forces. It lacks, therefore, the action of a monitoring feed-back from the environment. Consequently there is a deficiency of autonomic nervous system controls when the fœtus is in a resting, unstressed situation. It is as if the fœtal heart were like that in a heart-lung preparation, subject to its intrinsic controls on a chemical basis unless the autonomic system is called

into play by sensory input from its environment. The fœtus does possess from a time early in development the capacity for well-characterized patterns of behavioural (dynamic) responses, as Coghill[14] and Hooker[15] have shown, although Windle[1] is of a different opinion regarding their nature.

After delivery in those species that are mature at birth antigravity input to the central nervous system is established rapidly. It appears, therefore, that such sensory input to the central nervous system is an essential factor in contributing to sustained autonomic system output, at least so far as cardiovascular homeostasis is concerned. The effect is one of negative refection mediated by the parasympathetic system. This problem is part of the larger one of sensory deprivation in general on the body.

How effective homeostasis will be after birth must vary with the degree of morphological maturity at birth. Opossums, hamsters, mice, rats, rabbits, kittens, puppies, piglets, human babies and many other species will lack the capacity for homeostasis at birth because they do not respond to gravity. Others, such as guinea pigs, foals, lambs, calves, kids, and many other species will possess to a marked degree the capacity for effective homeostasis since they can stand, walk (or run) and regulate fairly well their body-temperature when they are born. Most notably, they possess a capacity for proprioceptive input to the central nervous system when they are delivered from a condition of weightlessness during development.

It is significant that the uterus is the original space capsule of mankind, and that all men have, so to speak, been in weightless orbit before they were born.

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TRANSAMINATION AND THE CONTROL OF MITOCHONDRIAL PATHWAYS

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RECENT work in several laboratories has demonstrated that the most important pathway for glutamate oxidation is via transamination and oxidation of α-oxoglutarate[1,2]:

$$\text{oxaloacetate} + \text{glutamate} \rightarrow \text{aspartate} + \alpha\text{-oxoglutarate}$$

$$\frac{\alpha\text{-oxoglutarate} + 1\tfrac{1}{2}\ O_2 \rightarrow \text{oxaloacetate} + CO_2}{\text{glutamate} + 1\tfrac{1}{2}\ O_2 \rightarrow \text{aspartate} + CO_2}$$

Jones and Gutfreund[3] have shown in their detailed work on guinea pig liver and mammary gland mitochondria that under *in vitro* conditions liver mitochondria oxidize some glutamate via glutamic dehydrogenase, but that the above transaminase pathway is more important and the latter is probably the only pathway under physiological conditions. Mammary gland mitochondria have no detectable glutamic dehydrogenase activity[2,3] and yet they oxidize glutamate at approximately the same rate as liver mitochondria. These findings indicate that the concentrations, activities and specificities of mitochondrial transaminase are most important data for the analysis of the control of mitochondrial metabolism.

We shall attempt to present a discussion of: (1) the concentrations of transaminase and other enzymes in various mitochondria; (2) the relation between transaminase concentration and the concentrations of pyridine nucleotide - linked enzymes in mitochondria; (3) some special aspects of the enzyme kinetics of transaminase; (4) the so-called latency of mitochondrial transaminase and its relation to the control of pathways in intact respiratory particles.

The purpose behind a detailed examination of various enzyme systems in the pure isolated form and in intact respiring mitochondria is to differentiate between various possible factors which control the direction and intensity of multi-enzyme pathways from junction points. A thorough knowledge of an isolated enzyme under various conditions and data on the behaviour of this enzyme in mitochondria should give information about the conditions and surroundings of this enzyme in respiratory particles. To get a complete picture of chemical organization in mitochondria in this way is necessarily a long-term programme; but some of the investigations reported here are intended to illustrate this approach to the transaminases of mitochondria and their relation to the enzymes of the citric acid cycle. More details of similar work on enzymes of the citric acid cycle are reported elsewhere[2,3].

Enzyme Concentrations in Mitochondria

Investigations on the concentrations of various active components of mitochondria from different tissues are too numerous to be referred to individually. Bucher and Klingenberg[4] review data on enzyme and coenzyme concentrations, Birt and Bartley[5] discuss pyridine nucleotide movements in mitochondria, and Estabrook and Holowinsky[6] discuss the cytochrome content of various mitochondria. The present investi-

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gation was carried out to provide data on the concentrations of a number of enzymes from assays on the same mitochondrial preparation, which has also been used for work on intact mitochondria as discussed below and elsewhere[3].

Table 1 contains results for the assay of activities of a number of mitochondrial enzymes at 25° under specified conditions. All the assays were performed on samples of preparations of mitochondria which were first used intact for respiration experiments[3]. Three samples of rat liver mitochondria were kindly provided by Dr. W. N. Aldridge. These samples were frozen at −20° and just before use they were diluted ten times and aliquots of such disrupted mitochondria were added to appropriate reaction mixtures and the rates of the oxidation or reduction of NAD (nicotinamide–adenine–dinucleotide) or NADP (nicotinamide–adenine–dinucleotide–phosphate) were followed spectrophotometrically at 340 mμ. The transaminase assays were coupled to dehydrogenases in the following manner:

(1) aspartate + α-oxoglutarate → oxaloacetate + glutamate

the rate of oxaloacetate formation was determined by following the rate of oxidation of NADH (reduced nicotinamide–adenine–dinucleotide) in the presence of excess malic dehydrogenase. In broken mitochondria the endogenous concentration of malic dehydrogenase was sufficient for this assay.

(2) oxaloacetate + glutamate → aspartate + α-oxoglutarate

The rate of α-oxoglutarate formation was determined by following the rate of oxidation of NADPH (reduced nicotinamide–adenine–dinucleotide phosphate) in the presence of ammonia and excess glutamic dehydrogenase. Glutamic dehydrogenase will oxidize NADPH at approximately half the rate of NADH, while the oxaloacetate reduction in broken mitochondria was completely specific for NADH.

At this stage the data obtained for the activity of transaminase, glutamic dehydrogenase, isocitric dehydrogenase and malic dehydrogenase are mainly of comparative interest. To establish the absolute concentration of these enzymes one has to find out whether their possible latency—which is discussed later—has been completely overcome and whether there are any significant losses during preparation of the samples of broken mitochondria. We have found that transaminase as well as glutamic and malic dehydrogenase are still partially bound to particulate material while the isocitric dehydrogenase is in a freely soluble form. The latter observation is of some significance in connexion with the variability of isocitrate oxidation by mitochondria, especially in the case of 'leaky' particles such as those prepared from mammary gland.

For the calculation of the percentage concentration of individual enzyme protein in mitochondria the activity per mgm. of pure enzyme has to be known. None of the enzymes discussed has been purified from guinea pig or rat liver, but a preliminary estimate is of considerable interest. Assuming for the rat liver enzyme the turnover and molecular weight of pig heart isocitric dehydrogenase[7] one can calculate that 2·5 per cent of the protein of rat liver mitochondria and twice this amount of guinea pig liver mitochondria consist of this enzyme. Similar calculations for the other enzymes estimated give values of the same order of magnitude.

We were particularly interested in the relative rates of the dehydrogenases, respiration and transamination. The relation between enzyme concentrations and respiration is discussed elsewhere[3]. Here we shall concern ourselves with the question as to how the concentration and kinetic characteristics of transaminases fit in with the observations on mitochondrial metabolism of glutamate, aspartate, α-oxoglutarate and oxaloacetate.

Table 1. Some Enzyme Activities of Disrupted Mitochondria and their Relation to the Rate of Respiration of Intact Mitochondria

Reaction	Rat liver	Guinea pig liver	Guinea pig mammary gland*
Glutamate + oxaloacetate to aspartate + α-oxoglutarate	1·2, 1·0, 0·92	1·0, 0·5	0·8
Isocitrate + $NADP^+$ to α-oxoglutarate + CO_2 + NADPH + H^+	0·14, 0·13, 0·13	0·21, 0·41, 0·31, 0·54	0·1
α-Oxoglutarate + NH_4^+ + NADH to glutamate + H_2O + NAD^+	0·16, 0·17, 0·19	0·18, 0·30	none
α-Oxoglutarate + NH_4^+ + NADPH to glutamate + H_2O + $NADP^+$	This reaction proceeded at about 55 per cent of the rate of the reaction in the presence of NADH		none
Glutamate + H_2O + NAD^+ to α-oxoglutarate + NH_4^+ + NADH	0·081, 0·035, 0·074	0·03, 0·08, 0·06, 0·04	none
Glutamate + H_2O + $NADP^+$ to α-oxoglutarate + NH_4^+ + NADPH	This reaction proceeded at about 55 per cent of the rate of the reaction in the presence of NAD^+		none
Malate + NAD^+ to oxaloacetate + NADH + H^+	0·36, 0·28, 0·30	0·06, 0·0925	
Oxaloacetate + NADH + H^+ to malate + NAD^+	3·25, 2·75, 2·98, 3·95	2·50	0·6, 1·4, 0·8
Respiration-rate of intact mitochondria in the presence of ADP, inorganic $PO_4^{=}$ and citric acid cycle substrates	0·12–0·14	0·04–0·05	0·04–0·05

The results given in this table are in μmoles of substrate utilized per min. per mgm. mitochondrial protein at 25° C. under conditions of optimum pH, substrate, coenzyme and metal ion concentrations, with the exception of NH_4^+ during glutamate formation which was 3·33 m*M*.
* Examination of the supernatant obtained after centrifugation of mammary gland mitochondria indicates considerable leakage of enzymes from these respiratory particles.

Kinetic Characteristics of Transaminase

Two types of enzyme preparations were used for kinetic measurements on various transaminase reactions. The transaminase of mitochondria from guinea pig liver and mammary gland and from rat liver were examined in suspensions of broken mitochondria as used for the enzyme assays described above. Secondly, we used a highly purified preparation of transaminase from pig heart, which corresponded to that described by Jenkins, Yphantis and Sizer[8]. This gives a basis of comparison with an enzyme preparation most extensively described in the literature. The kinetics of transaminase catalysis can be described by the scheme shown in Fig. 1, in which each step is reversible.

This scheme is formally the same as that described by Gutfreund and Sturtevant[9] for hydrogen transfer via enzyme-bound flavin adenine dinucleotide, but the rates of the individual steps of the transaminase reaction are so much faster that even rapid reaction techniques have so far only helped to confirm an order of magnitude for the rates involved.

It has been shown[10] that the reaction of the pyridoxal enzyme from pig heart with alanine to form pyridoxamine enzyme and pyruvate is fairly slow (half-time approximately 6 min. with alanine 2×10^{-2} *M*); the reverse reaction with pyruvate is at least 100 times faster. The reactions of the pig heart enzyme with aspartate or glutamate was known to be much more rapid but no attempt had previously been made to determine its rate. We have made some preliminary observations on the rate of forma-

XUM

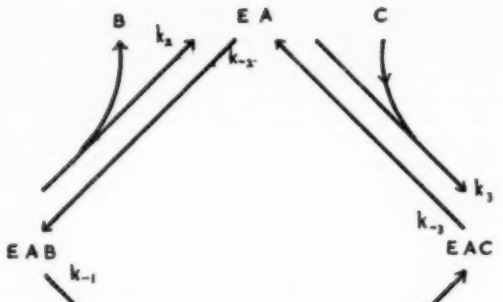

Fig. 1. *E*, pyridoxalphosphate enzyme; *AB*, amino-acid substrate; *EAB*, Michaelis complex; *B*, ketoacid product; *EA*, pyridoxaminephosphate enzyme; *C*, ketoacid substrate; *EAC*, Michaelis complex; *AC*, amino-acid product

tion of pyridoxamine enzyme in the presence of 0·05 *M* aspartate. The reaction was followed in a rapid-reaction spectrophotometer at 365 mμ. The method used was only capable of giving an approximate value for the half-time of the reaction (5 m.sec. at 25°). The difficulty of obtaining accurate kinetic constants is due to the fact that the earliest observation is made at a time at which the reaction is about half-way completed and the complication of the reverse reaction discussed later puts special demands on accurate observations over the whole time course of the reaction. It is, however, of great interest to get this approximate value for the velocity of the very rapid pyridoxamine enzyme formation, especially in view of the fact that this reaction is characterized by k_2 (see Fig. 1), which will be shown to be the smallest of four forward reaction constants. The following calculation is of interest, though it is based on a number of approximations. Jenkins and Sizer[11] give the results of an experiment designed to study the equilibrium:

$$\frac{\text{(enzyme-pyridoxamine) (α-oxoglutarate)}}{\text{(enzyme-pyridoxal) (glutamate)}} = K$$

The data given over a wide range of the two forms of the enzyme do not fit any simple model of a reversible reaction, but at low glutamate concentration one can conclude that the rate of the reaction of the pyridoxamine enzyme with α-oxoglutarate is approximately 100 times as fast as the reaction of the pyridoxal enzyme with glutamate. In any discussion of metabolic control at the point of one enzyme, one is concerned with the relation between the Michaelis constant and the steady-state concentration of the substrates. If two substrates—donor and acceptor—can influence the rate, then one is also concerned with the conditions under which the concentration of one or the other of these determines the rate of the overall reaction. The tissue concentrations of α-oxoglutarate are usually much lower than those of glutamate and the concentration of oxaloacetate is only of the order of 10 μ*M* [1,12]. The value for *Km* for oxaloacetate with mitochondrial transaminase is therefore of particular interest. We have determined this in the following manner with our rat liver mitochondrial preparation. The assay for glutamate to oxaloacetate transamination was carried out over a range of substrate concentrations under initial conditions of equal amino donor and amino acceptor concentrations.

After the optimum substrate concentration (5×10^{-3} *M*) had been determined a series of experiments at constant glutamate concentration (7×10^{-3} *M*) and a range of oxaloacetate concentrations ($0{\cdot}83 \times 10^{-4}$ to $1{\cdot}67 \times 10^{-3}$ *M*) was carried out. The *Km* for oxaloacetate was found to be approximately 9 μ*M*. At high oxaloacetate concentrations (above 5×10^{-3} *M*) inhibition of the transfer reaction occurs. This inhibition is of no biological significance since oxaloacetate is a very potent inhibitor of succinic and malic dehydrogenase at much lower concentration and could never build up to this level. It is, however, important to take this inhibition into account when kinetic investigations are attempted with less sensitive assay procedures.

A series of determinations of *Km* for the aspartate to α-oxoglutarate transamination were carried out with mitochondrial preparations from guinea pig liver and mammary gland and the purified pig heart enzyme. When the acceptor and donor concentrations are equal the following values for *Km* are obtained: guinea pig mammary gland, 1·15 m*M*; guinea pig liver, 0·77 m*M*; pig heart transaminase, 4·0 m*M*.

When the α-oxoglutarate concentration is reduced below that of aspartate, no significant reduction in the rate of the reaction is observed until the acceptor concentration is one-tenth of the donor concentration. This indicates that during the conditions of the *Km* determinations the reaction of aspartate with the enzyme is rate determining and the *Km* for the α-oxoacid is much lower than that for the amino-acid. This is analogous to the relationship between glutamate and oxaloacetate discussed above.

Latency and Metabolic Control

The latency of dehydrogenases in intact mitochondria has recently been discussed by Bendall and de Duve[13], and Boyd[14] describes similar phenomena for mitochondrial transaminase. In the report[14] on transaminase it is concluded that the activity for transamination from aspartate to α-oxoglutarate is increased up to three-fold on disruption of mitochondria. The following phenomena can be responsible for the so-called latency of transaminase and perhaps also of other mitochondrial enzymes.

(1) *Compartmentation and permeability* may make available only limited amounts of substrate to the enzyme and may select preferentially either internally generated or externally added substrates. Local accumulation of substrates and/or products can either accelerate or inhibit.

(2) *Structural alterations* of enzymes bound to mitochondrial enzymes or concentrated within compartments can also affect their activities. Several non-mitochondrial enzymes are known to be less active when they aggregate in solution. Fasella and Turano[15] have shown that transaminase forms a dimer with a dissociation constant of 10^{-8}–10^{-7} *M*. The dimeric form has only about 5 per cent of the activity of the monomeric form. Glutamic dehydrogenase, on the other hand, dissociates under a variety of conditions to form inactive sub-units[16]. It appears, however,

that many of the enzymes discussed are, at least partially, bound to the structural material of mitochondria and one has to be cautious in accepting that the conditions causing structural changes in enzyme molecules in free solution would cause similar changes in the bound form of the enzyme.

Under physiological conditions a number of factors must co-operate in primitive control of mitochondrial pathways. This is the type of control not involving the formation of new enzyme protein. The transaminase activity of mitochondria is more than sufficient to convert all the oxaloacetate which can be produced by the citric acid cycle into aspartate, provided a reasonable concentration of glutamate (0·1–1 m*M*) reaches the transaminase. The results of the present investigation show that the enzyme concentrations, kinetic parameters as well as the relation between oxaloacetate concentration and *Km* are consistent with the pathway for glutamate oxidation outlined in the introduction. If it were indeed true that all the oxaloacetate is converted into aspartate, which in turn is used for the biosynthesis of proteins and nucleic acids, then the citric acid cycle would be disrupted. There is insufficient information about the potential activity of condensing enzyme and about its affinity for oxaloacetate to predict whether the condensation reaction can compete successfully for oxaloacetate with the transamination system even in the presence of glutamate.

The elucidation of the control of the citric acid cycle and of its supply of substrates and disposal of products is both extremely important and, because of its many complex control points, a great intellectual challenge. This problem will be readily soluble when the type of information discussed for some enzymes in this article has been obtained for all the enzymes concerned and when tracer kinetic investigations with labelled intermediates have given full information about the relative availability for intramitochondrial enzyme reactions of externally added and internally generated substrates and products.

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DIAPAUSE IN AN AQUATIC MYMARID

By Miss D. J. JACKSON

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CARAPHRACTUS CINCTUS Walker parasitizes the eggs of various Dytiscidae[1] and is easy to rear in captivity on the eggs of the water beetle *Agabus bipustulatus* L. The entire development of this mymarid occurs under water within the host egg, the shell of which is transparent. The larvæ, usually 2 or 3 in each egg, are clearly visible during their later stages, so the time of pupation is easily determined.

Four to five generations of *Caraphractus* have been bred in a year in an unheated north room with a large uncurtained window at my house in St. Andrews. The last generation of the year undergoes diapause in the full-grown larval (prepupal) state. Such diapausing larvæ may be found in some eggs in September and usually in all eggs by the end of October. Pupation occurs in the spring and the majority of the adults emerge from March to May. The eggs of *A. bipustulatus* do not diapause but develop at all times of the year when the temperature is suitable.

In some parasitic Hymenoptera which diapause in the last larval instar[2,3], it has been found that maternal physiology may influence the incidence of diapause in the offspring, either by diet[2,3], by ageing of the females[3], or by rearing the females at low temperature[2,3]. In *Caraphractus* the adult female has never been seen to feed, and observations on the laying of old females previously deprived of host eggs showed that retention of the eggs in the ovaries of this insect (which has a very short adult life) was not a factor promoting diapause in the offspring. By exposing host eggs at various stages of parasitism to low temperature (5° C.) in August, development was retarded, but there was no diapause in the chilled generation and no increase in diapause in the offspring.

A succession of generations was obtained during the 'diapause season', September–March, by rearing *Caraphractus* in a constant-temperature room at 17·5° C. in continuous fluorescent light of 9 ft.-candles, each generation developing in a little more than three weeks, normally without diapause (Table 1, exp. 2). When host eggs with young larvæ were transferred from this constant-temperature room to the north room where diapause normally occurs, the majority of the larvæ went into diapause, while the reverse experiment (moving parasitized eggs from north room to constant-temperature room) resulted in direct development of all the larvæ. When females, reared in this constant-temperature room, were transferred to the north room to breed, they produced, from the middle of September to the end of December, 98·1 per cent diapausing offspring in 264 parasitized eggs. Since the temperature of the north room, though variable, was mostly 14°–16° C. and so not very much lower than the constant-temperature room, it seemed probable that the long hours of darkness at this season were responsible for inducing diapause in the developing larvæ.

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Table 1. Photoperiod Experiments with *Caraphractus cinctus* Walker

Ref. No.	No. of separate experiments	Temperature (°C.) av. min. / av. max.	Dates experiments were started	Hr. of light (tungsten)	Intensity of light (ft.-candles)	Hr. of darkness	No. of host eggs with direct developing parasites	No. of host eggs with diapausing parasites	Percentage of eggs with diapausing parasites
1	2	17·5 C.T.R.	Dec. 29, 1960	24	0·9	0	35	0	0·0
2	52	17·5 C.T.R.	Aug. 1960–Feb. 1961	24	9·0	0	467	2	0·4
3	3	13·5/14·5	Nov. 23–25, 1960	24	8·0	0	63	0	0·0
4	2	25/26 C.T.R.	Nov. 4, 1960	24	12·0	0	17	0	0·0
5	5	13·0/16·5	Feb. 21–March 8, 1961	20½–21	8·0	3–3½	105	1	0·9
6	6	14·0/15·0	May 16–28, 1961	19	7·75	5	209	0	0·0
7	10	13·0/17·5	Jan. 26—Feb. 5, 1961	15	42·0	9	20	187	90·3
8	12	12·0/14·5	Dec. 16, 1960–Jan. 18, 1961	14	8·0	10	5	239	97·9
9	5	17·0 C.T.R.	Jan. 11–14, 1961	8	7·5	16	0	27	100·0
10	11	13·5/15·5	Dec. 15, 1960–Feb. 12, 1961	7½–8	8·5	16–16½	0	206	100·0
11	5	15·2/17·2	June 28—July 9, 1961	7½	7·75	16½	0	173	100·0

C.T.R., constant temperature room.

Experiments with different photoperiods were then tried, first by exposing newly parasitized eggs during December to daylight from a north window and supplementing this with artificial tungsten light of 30 ft.-candles in the evening, a method similar to that used for mosquito larvæ by Baker[4]. The temperature averaged min. 10·5°, max. 13·5° C. With only 3 hr. of artificial light, all the larvæ went into diapause; with 6–6½ hr. of artificial light the diapause was 88·3 per cent, though the total light (including morning twilight) was about 15–16 hr. Controls, covered during artificial light, gave 97 per cent diapause. Further experiments, some in ventilated tea-chests and others in constant-temperature rooms, showed that direct development occurred during continuous light, or with 3–5 hr. of darkness (Table 1, exps. 5 and 6).

The effect of a short photoperiod (7½ hr.) in promoting diapause from ovipositions in April and May has recently been demonstrated, for 98·6 per cent of 306 parasitized eggs so treated went into diapause, while 221 controls, exposed to daylight in the same (north) room at the same time, have all given direct developing *Caraphractus*.

Experiments have been undertaken to find out the lowest intensity of light required during the night to prevent diapause. By using daylight from a north window in February and March and two 5-W. neon bulbs all night from 4.30 p.m. to 8.30 a.m., and placing 264 parasitized eggs at varying distances from the light, direct development of all the parasites occurred, though the light they received at night was only 0·03–0·3 ft.-candle. Controls kept in the same room, in darkness during artificial light, gave 82·5 per cent diapause. The temperature averaged min. 12·5°, max. 15·5° C. Three further experiments were conducted in the spring in tea-chests, using for 15 hr. a tungsten 25-W. bulb giving 12 ft.-candles and for 9 hr. cresyl blue filters adapted to give light intensities of 0·8, 0·25 and 0·05 ft.-candle. As a result, all the successfully parasitized eggs in each experiment (a total of 513) gave direct developing *Caraphractus*. The average minimum and average maximum temperatures in these three experiments were 13·5° C. and 16·5° C.

These results show that *Caraphractus* is sensitive in the larval state to light of extremely low intensity. It seems likely that in ponds direct development will only occur with long daylight hours combined with faint light at night (twilight), or with a few hours of darkness. In other insects[5–8], long day-lengths at medium temperature promote direct development; with *Caraphractus*, 9 hr. of complete darkness suffice to induce diapause in the great majority of specimens (exp. 7). Experiments have shown that low temperature in this insect is not the deciding factor, and in autumn, when reared in the north room, with an open window, diapause started before the cold weather set in. At the commencement of the 'diapause season' there is individual variation in the susceptibility of the larvæ; and eggs, parasitized by the same female within 5 min. of each other, may yield either diapausing or non-diapausing *Caraphractus*. Moreover, it sometimes happens that the development of two individuals within the same host egg may be of both types, though the eggs producing them were laid at one thrust of the ovipositor. This variation disappears as the hours of darkness lengthen.

From May until August direct development normally occurs and this coincides with the long twilight of the summer nights and the absence of astronomical darkness. The onset of diapause in the autumn sets in at a time when there are about 6 hr. of astronomical darkness, which increases in early October to more than 8 hr.; this may well be the 'clock'[9] to which the larvæ respond. Once in diapause, *Caraphractus* can withstand some desiccation, even if the host eggs collapse during drought. Diapausing larvæ can also survive for days in freezing water (0–1 to 0–3° C.) and when removed to a suitable temperature, pupation may occur promptly. When the larvæ are not subjected to frost, the diapause runs its course and usually extends over several months, but is sometimes greatly prolonged.

The experiments in the constant-temperature rooms were carried out in the Natural History Department of the University of St. Andrews and I am grateful to Prof. H. G. Callan for affording me these facilities and to Dr. C. Muir for the valuable help he has so generously given me with technique and light measurement. Prof. and Mrs. Stibbs have kindly provided me with useful information regarding the duration of astronomical darkness in the latitude of St. Andrews.

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HUMANITIES OF SCIENCE

Science since Babylon

By Prof. Derek J. de Solla Price. Pp. x + 149. (New Haven, Conn., and London: Yale University Press, 1961.) 4.50 dollars. 37*s.* 6*d.*

THIS book, Prof. Price tells us, had its origin in a set of five lectures given under the auspices of the Department of History at Yale University in 1959. It makes no claim to be a history—even a historical sketch—of 'science since Babylon', but rather by reflecting on certain special aspects of that history to gain some insight into why, or in any event how, science has come to be what it is; and thence to deduce the likely course of its future development. The whole thus constitutes an essay in what Prof. Price wishes to call "the humanities of science".

In five chapters the author approaches the question along three fairly distinct roads: the thesis that the character of a scientific epoch is largely conditioned by the instruments available, hence by the special skills of the contemporary 'practitioners'; a somewhat detailed examination of the great 'mutation' in physics consequent on Roentgen's discovery of X-rays; and a roughly statistical analysis of the growth of science deduced from such 'pointers' as primary periodical publication, abstracts, individual papers, numbers of active scientists and universities.

Despite Prof. Price's well-known virtuosity in the first field, here amplified by some fascinating 'revelations' of his methods, belief in the thesis is not likely to be strengthened by some of the arguments which are adduced. What are we to make of the statement (pp. 51, 113) ". . . that it was the Germanic region of Luther rather than Catholic Italy that saw the revival of astronomy by Regiomontanus [d. 1476], Kepler and Copernicus"? Or by the description (p. 61) of Hooke as an ingenious artisan " . . . who though reasonably educated [Westminster School and Christ Church, Oxford] had no special training in science other than . . . by apprenticeship ['research assistant' to Willis and later Boyle]?" Who among the early Fellows of the Royal Society, we may ask, had a better preparation in 'science'?

On the other hand, Chapter 5, entitled "Diseases of Science", " . . . its superabundance of literature, its manpower shortages, its increasing specialization, its tendency to deteriorate in quality"—together with the epilogue, entitled "The Humanities of Science", constitute for the reviewer alike the most convincing analysis of the terrifying *djinn* that optimistic Western man has released from its bottle, and a carefully considered justification for the establishment of 'humanities of science'—call it what you will—as a separate discipline. For this reason *Science since Babylon* is an important, possibly a very important, contribution. It is all the more regrettable that it is exorbitantly priced.

W. P. D. WIGHTMAN

A SHORT HISTORY OF SCIENCE

The Mechanization of the World Picture

By Prof. E. J. Dijksterhuis. Translated by C. Dikshoorn. Pp. viii + 539. (Oxford: Clarendon Press; London: Oxford University Press, 1961.) 105*s.* net.

TRIPLY laden by its burden of price, bulk and title, this book cannot be expected to join the ranks of best-selling general histories of science. However, its contents should and probably will be made known to the ever-increasing audience for the history of science. Since the publication of Burtt's pioneering work some thirty-five years ago, the 'metaphysical' side of the rise of modern science has received increasing attention, and there is now a fair selection of popular books presenting this story. Up to now each author has had to dig for himself in the secondary literature, scattered among many journals and written in all the European languages. Now those who teach and write on the history of science have a coherent and scholarly account, written in English and with a comprehensive bibliography. There is no longer any excuse for ignorance. Also, those who want to learn something of the history of science and are not satisfied by vulgarization, however high, can study this book with profit and satisfaction.

Prof. Dijksterhuis gives us an example of how to write the history of science. In each of the many topics he covers, he describes briefly what he is going to discuss, and (more important) mentions relevant topics which he is not going to discuss. The history of science has been plagued too long by smash-and-grab methods where one 'scientific' contribution of a man is described and analysed, while the philosophical, religious or social thought in which the contribution was originally embedded is left unmentioned. Also, it is clear that he has thoroughly mastered the technicalities of each problem, and not contented himself with understanding only that part which could easily be popularized. This produces greater accuracy on small and large points. His is the only general account of seventeenth-century mechanics which mentions the significant fact that Newton's laws do not use time-derivatives; "$F = ma$", as an explicit statement, dates from Euler. Another example is his simplified diagram of the Ptolemaic world-system: no other such diagram shows both the deferents of the inner planets, and the epicycle-arms of the other planets, as roughly parallel to the line joining Earth and Sun.

The first half of the book is devoted to the background in ancient and medieval thought. The two most attractive problems, cosmological speculation and the causes of motion in inanimate bodies, receive their proper place in the complex of philosophical problems on the nature of reality and the nature of change. Prof. Dijksterhuis covers the whole range of the exact sciences and philosophical thought

in classical antiquity. He never describes a result without criticizing it, and from his criticisms emerges a coherent picture of the intellectual limitations of the 'science' of the time. He also has a good sense of what can be compressed, and what cannot; where the scientific technicalities are not important for the general story, they are pruned drastically (with a reminder of what is being left out); Aristotle's philosophy is given detailed attention, and the beautiful coherence of the whole system is exhibited clearly.

The section on scholastic 'science' is most illuminating. Through the work of Dr. Crombie and Prof. Clagett, we have been approaching a balanced appreciation of the achievements of this tradition, and developing general ideas on the causes of its fatal limitations. In each of his discussions Prof. Dijksterhuis illustrates the interpenetration of scientific thought with problems of logic, metaphysics, and theology. He also sketches in the medieval world-picture, and shows clearly how this conditioned the manner of approaching, and solving, scientific problems. The characteristic 'double-think' solution of the practical problem of the conflict of science with theology is described as well as can be done by a scholar living in a free society.

The second part of the book, on the Renaissance and the seventeenth century (concluding with Newton), offers somewhat less. We are not within sight of a synthesis of what happened between Oresme and Galileo; and on the development of mechanics in the seventeenth century there is already a fair literature. This is not to say that Prof. Dijksterhuis provides only well-worn material; his discussion of the continuous tradition in the problem of change and composition (What happens to the qualities of the original substances?) lights up untrodden pathways. But nowhere does he discuss in general terms the astonishing intellectual mutation which took place at the beginning of the seventeenth century, when a world-picture much like our own was suddenly conceived and propagated, rendering nearly irrelevant centuries of philosophical thought, and providing a framework in which modern science could be created.

It is unfortunate that the author was not able to revise the text (originally published in Dutch in 1950), for the present book is essentially based on work carried out in the 'thirties, with additions from the War and early post-war years. Much has been achieved in the history of science in the past decade; it is a tribute to Prof. Dijksterhuis's maturity of judgment that his history could be enriched, but nowhere seriously challenged, by more recent work.

J. R. Ravetz

COSMICAL LANGUAGE

Lincos

Design of a Language for Cosmic Intercourse, Part 1. (Studies in Logic and the Foundations of Mathematics.) By Dr. Hans Freudenthal. Pp. v+224. (Amsterdam: North-Holland Publishing Co., 1960.) 45*s*.

ONE needs must take seriously a monograph in the series Studies on Logic and the Foundations of Mathematics edited (*inter alia*) by so distinguished a mathematical logician as L. E. J. Brouwer. If its ostensible aim were self-evidently *en rapport* with the title of the series, the editors of *Nature* could have chosen few people more unfitted than myself to respond to a request to review it. Their only conceivable motive for doing so is that I once (ten years ago) gave, at its request, an address (*Astroglossa*) to the British Interplanetary Society on the theme which the subtitle of this monograph discloses. The recapture of echoes from radar signals transmitted to the Moon had then lately made conceivable, if none the less unlikely, intercommunication between ourselves and beings, if such there be, on Mars or Venus.

This was confessedly a *jeu d'esprit* for an evening's entertainment; but it had an undertone of serious intention, as there disclosed. Should contact between ourselves and extra-territorial occupants become possible, the success of the enterprise would be a challenge compelling us to retrace our steps from traditional methods of teaching existing terrestrial languages parrot-wise by paradigm or by repetition. We should indeed have to undertake an exacting revaluation of the semantics of so-called natural languages and of syntactical obscurities which do not impede communication between individuals who share explicitly, or at least implicitly, a common social context of discourse. However fruitless *vis à vis* the ostensible outcome, the undertaking might therefore prove to be worth while: if it put the spotlight on semantic refinements we should advisedly incorporate it in an ideally constructed global auxiliary; or if it exposed defects of imparting instruction in a so-called natural language if adopted as a medium of international communication.

Accordingly, I would be the last to dismiss as crackpot a project so grandiose as *Lincos*. Dr. Freudenthal and I at least have common ground with respect to the initial stages of the programme. If we postulate the existence of hypothetical extra-terrestrial beings at least as intelligent as ourselves, our only common denominator of communication in the first phase of a protracted tuitional process would be the integers. Whence we may conceivably proceed by easy stages from conveying simple algorithms to non-visual geometry, for example, by exemplary definition of a radio signal *and so on and so on* to specify trigonometrical ratios as infinite series. How far the introduction of the symbolical logic of Dr. Freudenthal would help engineers on the job to carry out this assignment is not fully clear to me; but I concede that I dismissed lightly as too obvious the theme of a second stage here set forth by himself in a symbolism tailored as elsewhere to the Russell–Quine tradition of logistic. Following stage 1 (that is, the domain of mathematical discourse), Dr. Freudenthal devotes a chapter to the concept of time. Here he proposes that we can make use of varying signal frequencies to establish what we each adopt as our units of time, whence *pari passu* our concept of frequency.

Thereafter, Dr. Freudenthal (whose next chapter is "Behaviour", that is, relations involving different individuals at the transmitting or at the receiving end) parts company abruptly with me. I have stated, and still hold, that the next imaginable step would be to establish a common factual framework of semantic reference. At this stage, the only common field of factual experience which the parties could explore would be celestial occurrences (for example, eclipses, conjunctions and occultations); and this our vocabulary of time signals would have now made practicable. Thereafter, we might conceivably learn to convey the

structure of our several planetary crusts and atmospheres in terms of spectrum frequencies. It seems to me that the last topic about which we could hope to achieve understanding would be the actions of persons in general, and the concept of the ego in particular.

How Dr. Freudenthal sidesteps this hurdle, I do not follow. It may be that he will make himself more intelligible later in Part 2. However, in justice to him, one must here say that his main pre-occupation is not with the factual sequence of the tuitional process. In accordance with the aim of the series in which the monograph appears, his paramount concern is to equip the syntax of interplanetary (or intergalactic) communication with a symbolism consonant with the requirements of a two-valued logistic rejected by some mathematicians in the forefront of bull-dozing the foundations of mathematics as such and (in my view) totally inadequate for the requirements of the biological sciences. The outcome may usefully confer on symbolic logic an agreeably topical flavour for the relief of students compelled to take an examination in the subject. From any other point of view, Dr. Freudenthal has failed to convince me that his programme is very profitable; and my reluctance to concede that it is so gains force from two considerations.

One is that examples cited to show how symbolic logic makes manifest semantic and syntactical pitfalls of common speech are not unfamiliar to students of comparative linguistics, who draw on a much richer (and more relevant) fund of material. The use of two particles of relation should make this sufficiently clear. In Teutonic and Romance languages we have one word for our *always* (German *immer*, Swedish *altijd*, French *toujours*); but Welsh distinguishes *bob amser* (= *each time*) from *yn wastad* (= *ceaselessly*). Again English *with* and French *avec* cover both Welsh *ag* (= *by means of*) and *gyda* (= *in the company of*).

Another doubt will disturb the reader who is unrepentantly sceptical about the extent to which logistic can make the semantic and syntactical deficiencies of common speech more explicit than can the study of comparative linguistics. On p. 104 ("Behaviour") we meet:

$$\text{Ha.Inq.Ha}\cdot\text{—.}t_1t_3\ \text{Hb Enu.?} = \text{.Car Etc}$$

$$\text{Sed}\ t_1t_3\text{.Hb.Cpu}\cdot\ \text{?} = \text{.Car Etc}$$

The intention in this context is to introduce a distinction between two uses of *but*, symbolically denoted TAN (Lat. *tamen*) and SED (Lat.). Do we have to invoke logistic analysis to do so? Assuredly no. Dr. Freudenthal has to explain this distinction in the text through the medium of common speech, but it will not necessarily be front-page news to a philologist or classical scholar already familiar with *tamen* and *sed*. Since the engineer will have to recode in appropriate radio signals any symbols in which we formulate our curriculum of interplanetary (or intergalactic) tuition, all that is relevant to the credentials of what we use is whether the terms and constructions conform to the requirements of rigorous semantic rectitude. If so, it is therefore difficult to see why we should add to his or her difficulties by using an unfamiliar code for what a more familiar one could do equally well with a little premedication.

LANCELOT HOGBEN

A ROMAN CATHOLIC VIEW OF EVOLUTION

Evolution and Christians

By Philip G. Fothergill. Pp. xix + 15 plates. (London: Longmans, Green and Co., Ltd., 1961.) 42s. net.

DR. FOTHERGILL, in addressing his fellows of the Roman Church on the matter of evolution, has undertaken an important and difficult task, and has carried it out with a meticulous thoroughness and a scrupulous integrity. His book is an encyclopædia of information about the history, progress and present position of the case for evolution so far as this can be stated within the strict limit of Catholic dogma. He has presented with a wealth of detail the familiar story of Darwin's evidence in the *Origin of Species*, of the subsequent developments in taxonomy and palæontology, of the impact of genetics and of the varied fields of study since involved. He has then dealt at even greater length with heredity, the matter of chromosomes, genes, and mutations, with the relevance of cytology and serology, and with innumerable records of experiments with *Drosophila*. Finally he discusses problems of isolation, of the effects and limitations of selection and of hybridization, and faces the question how far does all this elaborate and highly technical research enable us to point to the appearance of new species arising under the conditions of neo-Darwinian theory and precisely scientific control.

In these long and difficult records he does his best to state and expound the innumerable polysyllabic names that each research department applies to its subjects—a heroic task which makes his book almost incomprehensible to the layman—to furnish it with good and relevant diagrams and illustrations, and to insert quotations, short and long, from a large number of writers more or less well known. He also quotes a few critics of his views, especially Dr. Douglas Dewar and Prof. G. Gaylord Simpson. He is himself very ready to admit that much of what he describes is inconclusive—some of it is also irrelevant. His own final conclusion appears to be that though the mass of data give a strong case for accepting evolution as a hypothesis, the only clear examples of new species recent or demonstrable are those of allopolyploidal plants and fertile hybrids like the common hemp-nettle or Townsend's cord-grass—our notorious enemy in the battle of the Western Approaches.

The fact is that his task as limited by Catholic orthodoxy is scarcely possible, and that for three chief reasons. First, he realizes and complains that without a philosophy of science it is impossible to relate evolution to any coherent interpretation of the world as we know it; the details which he reports so carefully become trivial and meaningless. Yet he is debarred by ecclesiastical authority from making any reference to philosophic evolutionists unless, like Sir Julian Huxley, they are avowedly hostile to the faith or like the one or two unknown Catholics whom he quotes accredited by it. It is astonishing for an Englishman who has spent all his life with the problems of evolution to read a book on it in which there is not a single mention of Bergson or Lloyd Morgan, Samuel Alexander or A. N. Whitehead, of emergence or of holism or any other of the systems which have interpreted the process and made the details meaningful.

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Secondly, and presumably because of the dogma that "animals have no souls", he never touches on the large and exciting field of comparative psychology, or on the evolution of the behaviour-patterns and instinctive responses which mankind has so obviously inherited and to which all post-Freudian analysis has directed attention. The idea that each and every "intellectual soul" of man is a special divine creation if tenable must surely be adjusted now so as to allow room for an age-old substratum of animalisms conditioning our mind and morals as they do our bodies.

Thirdly, he writes always within the strait-jacket of Papal orthodoxy, much of it formulated in pre-Copernican and all of it except one encyclical in pre-Darwinian days. Though much of this may be held to deal with matters outside the range of present-day science, it has, even so, corollaries of dogmatic status, for example, the historicity of Adam and Eve, which bear directly on his theme. Moreover, does he really think that in matters demanding not only religious but also scientific, historical and ethical experience, the Vatican is the proper and infallible authority to which every other expert must yield unquestioning obedience?

CHARLES E. RAVEN

CLIMATES OF THE PAST

Descriptive Palaeoclimatology

Edited by A. E. M. Nairn. Pp. xi+380. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1961.) 11 dollars; 80*s*.

GEOLOGISTS who have struggled to interpret past climates will welcome this book for its wealth of factual information and for the critical way in which most of the authors have approached their special interests.

The first chapter, apart from a brief introduction by the editor, is a summary by Lamb of the nature and causes of the world's climate to-day. It is not easy to read, but it is extremely informative. Then follows a series of chapters each written by a specialist and dealing with the separate criteria which can be used as a means of assessing at least some facet of climate. These may be pure physical measurements (palæomagnetism, the ratio of oxygen-16 to oxygen-18), geological observations (the dips of æolian sandstones, the evidence of the presence and extent of ice), physical chemistry (evaporites and red beds) or biological deductions (from vertebrate, invertebrate or plant fossils). Finally, there are four chapters in which are traced the climatic changes over a large part of geological time in Europe and North America, the Far East and Gondwanaland.

Flint, dealing with glaciation, perhaps stands on the firmest ground, for the conversion of water to ice has a well-known climatic relationship and the presence of glaciers or permanently frozen ground in many cases gives rise to conclusions about climate which are without ambiguity. Much more difficult to interpret are evaporites and red beds, and the authors of these sections are understandably cautious in their conclusions. This welcome attitude is indeed apparent throughout. In dealing with the oxygen isotopes, for example, Thorley does a great service in pointing out the assumptions which have to be made before this method can be used for temperature determinations—assumptions which can too easily be ignored by stratigraphers eager to use a physicist's measurements to support a theory.

Perhaps the biologists are the most cautious of the authors, for all stress the difficulty of using the present as a key to the past when ancient floras and faunas are specifically and generically so different from those of to-day. On the whole, the greatest reliance is placed on anatomy, for it seems that certain modifications of structure, similar in widely diverse creatures, are adaptations to certain extremes of climate.

Throughout the book, emphasis is placed on polar wandering and continental drift. The palæomagnetists accept it without question, for their results would be largely meaningless without it, but they still have a long way to go before they present a conclusive and agreed story. Thus Nairn's equator-positions for the Trias of Europe (Chapter 7, Fig. 9), Africa and North America (Fig. 7) seem to provide an insoluble problem of drift if his three lines are to join into a continuous girdle at one moment of time. The palæontologists are more non-committal about polar shift, while conceding the necessity for great climatic change in the present polar regions. Van Houten's examination of the significance of red beds tends to support wandering rather than static poles, but, on the other hand, Green feels able to explain the distribution of evaporites without recourse to drift or polar change.

As a whole, the book is a mine of information and both a stimulus to enthusiasm and a corrective to over-enthusiasm in approaching a difficult problem. Its copious references are international in character though scanty from beyond the Iron Curtain. It would be churlish to point out a few misprints and errors of translation and more to the point to congratulate the editor on welding together the contributions of fifteen authors from seven countries.

F. W. SHOTTON

BIRDS OF TROPICAL PARADISE

Birds of Trinidad and Tobago

By Dr. G. A. C. Herklots. Pp. 287+20 plates. (London: William Collins, Sons and Co., Ltd., 1961.) 42*s*. net.

THE islands of Trinidad and Tobago, the southernmost of the West Indian chain, have a combined land area of about 2,000 square miles, Tobago being very much the smaller, and at 10° N. and about 10 miles from Venezuela on the South American mainland, they are truly tropical. Being small islands they possess a high proportion of coastal land; in Trinidad there is a range of mountains (in the north) topping 3,000 ft. in two places, abundant deep forests, lowland plains, savannahs and extensive swamps; a wide range of habitats that encourage a wide variety of bird species both exotic and interesting.

Without undertaking an expensive safari (of the type so popular with programmers of television) one may seek out and enjoy the sight of a flock of flamingoes (*Eudocimus ruber*) either feeding in swampy land or, at sunset, a blaze of scarlet glory winging its way to roost—a sight not easily forgotten. I have, indeed, photographed a group of these birds feeding quietly on a plot of low-lying coastal land not two miles from the capital city, Port of Spain.

From the islands off the north-west peninsula one may film with ease the superb aerobatic displays of flocks of frigate-birds (*Fregata magnificens*—wingspan up to 7 ft.) as they swoop gracefully to snatch small fish from the surface of the sea with a downward flick

of the head, then wheel aloft again, frequently challenged in mid-air by their comrades eager to snatch their prize.

In the cool of the thick forests of Trinidad one may see the gaily dressed toucan (*Ramphastos vitellinus*) perched high in the tree-tops or hear its hard crackling call; or one of several parrots and parrakeets common in the forests. Even more spectacular are the brilliantly coloured macaws which may be found in and near the Nariva swamp. But one may have to look longer to discover the giant nightjar (*Nyctibius griseus*), which is rare and evasive, assuming an erect posture to simulate the elongation of its perch, when danger is nigh. It is said that a museum once offered £100 for one of its eggs. There is the fascinating guacharo or oilbird (*Steatornis caripensis*) to be found in the caves at Aripo and elsewhere. The oilbird nests from year to year in the same place on ledges high on the walls of the cave, so that a truncated cone of guano is built up, in the cupped top of which the new eggs are laid. The effect is of rows of artificial stalagmites. They feed on the oil-rich berries of certain palms and the young become veritable 'balls of fat' from this rich diet. When disturbed an alarm call, like "the cries of tortured men", rings through the cave. Being completely nocturnal they are provided with a form of 'radar' which enables them to move freely in the dark caves.

On the islet of little Tobago is another interesting ornithological attraction, for here may be seen the greater bird of paradise (*Paradisea apoda*), which was brought from the Aru Islands off Dutch New Guinea to this sanctuary by Sir William Ingram in 1909. His sons donated the island to the British Government on the condition that it be maintained, *in perpetuum*, as a bird sanctuary.

Then there is a group of what must be among the most beautiful of all birds—the hummingbirds (Trochilidae). Trinidad has for long been known as the 'land of the hummingbird' and it is re-assuring to hear from Dr. Herklots that there is little reason to suppose that they are not as abundant as ever. In all, 17 species are listed, of which Herklots has seen 15 in his seven years on the island. Some species are certainly very common and may be observed in gardens in the heart of town, flashing like priceless jewels in the strong sunlight as they sip nectar from flowers such as the ixora or Barbados pride (*Caesalpinia pulcherima*), hovering, humming, perkily prying at each bloom in an inflorescence, then . . . away, with incredible speed.

These are but a few of the 415, or so, birds described in this most welcome book. One may say that it has been awaited for half a century, since the last comprehensive, descriptive guide to the birds of Trinidad was written (in French) by A. Leotaud in 1866. While in its own way Leotaud's book is a classic, it could scarcely be said to be *au courant*, and is in any event rare and almost impossible to borrow. Unfortunately, Dr. Herklots' book does not bring us quite up to date as he has not managed to find a proportion of the birds listed in the book and has drawn heavily on Leotaud and on the publications of Sir Charles Belcher and G. D. Smooker, *On the Birds of the Colony of Trinidad and Tobago*, to be found in *Ibis* between 1934 and 1937. This in no way detracts from the practical utility of the present volume and Dr. Herklots must be congratulated on the efficiency and clarity of his presentation. The glossary, blessedly, precedes, instead of follows, the descriptions and there is a short introduction with two maps. For each species there is a precise description followed by notes on nidification, habitat, voice (not in every case), distribution and field identification. The plates illustrate some 260 species, about 180 in colour, and are, on the whole, very good indeed, but the majority are head-and-shoulders only. Since most of the species are also to be found on the neighbouring mainland, this book is a useful guide for English-speaking naturalists in Venezuela, the Guianas and Brazil; but above all to those interested in the birds of Trinidad and Tobago, this is now the guide of prime importance and, as such, an indispensable one, 'completing' Dr. James Bond's *Birds of the West Indies* which omits these islands. My only regret is that no photographs were included which would have given those who have not visited the islands some small impression of their charm.

L. B. QUESNEL

AN ARACHNOLOGICAL ANTHOLOGY

Spiders, Men, and Scorpions

Being the History of Arachnology. By Theodore H. Savory. Pp. 191+15 plates. (London : University of London Press, 1961.) 30*s*. net.

IN spite of their relatively small numbers, arachnologists have a liking for writing about each other as well as about their subject, and without doubt this has enriched the literature. We have already had biographical accounts by W. S. Bristowe and Pierre Bonnet, and Mr. Savory has now taken this a good deal further in his latest book.

He has again demonstrated his versatility as a writer in this history of man's relationship with spiders, scorpions and other arachnids, which begins with legend in Ovid's story of Arachne to the outstanding names in arachnology in modern times. The first book devoted entirely to spiders was apparently published in 1544 in Basle, but until the seventeenth century the literature appears to have added more in the way of superstitions to the knowledge of arachnology than original observations. The story of the development of tarantism, a curious disease which was supposed to be caused by the bite of the tarantula (*Lycosa tarantula*, a wolf spider), is full of interest, however, even though the mystery of how it came about remains. The distressing effects supposed to have been produced by the spider's bite could only be relieved by music and dancing, and to-day the only vestige which remains is a dance, the tarantella, probably one of the few contributions made by an arachnid to human culture.

Inevitably in a work of this kind a good deal of reference must be made to numbers of minor and insignificant writers for the sake of keeping the record complete. Occasionally this makes the reading rather tedious in spite of one's admiration for the industry of the writer in tracing historical data. Most of the great names which are familiar to modern students of arachnology are referred to in the later chapters of the book, and Mr. Savory's enthusiasm and style give a fresh and personal picture of people who to most of us have never been more than a name attached to monographs or scientific papers. The outstanding workers, such as Simon, Pickard-Cambridge, Koch and Thorell, worked mainly on the Araneida, and a good deal of the book is concerned

with work on this order. Mr. Savory considers that the foundation of spider taxonomy was laid by French and German students in the early nineteenth century, of which the publication of Hahn and Koch's *Die Arachniden* in 1831 was the most striking example. John Blackwall for Britain made a major contribution in 1861 with his Ray Society volume on *British Spiders*, and the three countries Britain, France and Germany perhaps remained pre-eminent in this field until recent times. Mr. Savory's review does not include post-1958 works and consequently misses H. Wiehle's monograph on the Micryphantidae, one of the most important taxonomic works since the War. He is perhaps a little unfair to the younger generation of German zoologists, which, he says, "has only just begun to appreciate the Arachnida as subjects for research". In fact, since 1942 more work has been carried out in Germany on the biology and ecology of spiders than probably any other country.

This and recent work in other countries emphasize an important historical point not made by the author that the taxonomy of European spiders is now at least sufficiently well known for the main interest of the younger generation of arachnologists to concern themselves largely with population and biological problems. This would appear to be the field of investigation for the future, although outside Europe, faunal surveys and taxonomic studies will continue to be necessary for many years to come.

E. Duffey

BRITISH MOTHS

The Moths of the British Isles

By Richard South. New edition, edited and revised by H.M. Edelsten, D. S. Fletcher and R. J. Collins. First Series: Sphingidae, Endromidae, Saturniidae, Notodontidae, Thyatiridae, Drepanidae, Lymantriidae, and Noctuidae. Pp. 427+148 plates. Second Series: Lasiocampidae, Arctiidae, Geometridae, Cossidae, Limacodidae, Zygaenidae, Sesiidae, and Hepialidae. Pp. 379+141 plates. (The Wayside and Woodland Series.) (London and New York: Frederick Warne and Co., Ltd., 1961.) 35*s*. net each volume.

INTENDED primarily as a guide to the identification of the larger British moths, this new edition of a standard work fulfils its function more successfully than the editions of 1923 or 1939 mainly through the introduction of improved and completely new colour-plates. The original paintings, from which the colour-plates were prepared, are with very few exceptions excellent. In the few copies of the new edition examined by me, however, the colour-plates do not always attain the same high standard as the artist's paintings: there is a lack of register in many plates and in several of them the red element is weak, resulting in unnatural greenish tones. In spite of these drawbacks the plates are far superior to those in any except the first edition, and several plates (especially those of the genus *Eupithecia* Curtis) are as good as any illustrations previously published in Britain. Many of the plate legends (for example, Series 1, plate 97) are unfortunately most confusing and will clearly have to be rearranged by the publishers in subsequent editions. References to the corresponding pages in the text have been omitted, as in previous editions, and numerous species exhibiting little sexual dimorphism continue to have both sexes illustrated. Of some significance is the introduction of references in the text to figures of the genitalia of some of the more difficult genera (for example, *Procus* Oken and *Hydraecia* Guenée), an indication that externally the species of these genera are extremely difficult to separate and that the colour-plates are of little use as a means of identification. The reproduction of many of the half-tone figures is very poor.

Since the publication of the first edition in 1907 the bulk of the text has remained unaltered and, although a thorough revision was clearly overdue, to remedy the haphazard and inconsistent treatment of many species, the opportunity to do this has not been taken. New text is therefore restricted mainly to passages of supplementary information; leaving most of the remainder almost exactly as it was more than half a century ago.

An important addition is the detailed treatment of several little-known moths, such as *Calamia tridens occidentalis* Cockayne. A further improvement is the adoption for the first time in this book of the correct form of scientific nomenclature in accordance with the International Code.

The unsystematic arrangement of the various families of moths is regrettable but, as the editors state in the introduction, this is the only way in which both plates and text could be arranged to avoid dividing the section on Noctuidae between the two volumes (a disadvantage of previous editions).

It is remarkable that in spite of the attention given to Lepidoptera by British entomologists, the editors have seldom been able to cite the sub-specific identity of the British representatives of a particular polytypic species—a result of the paucity of taxonomic work on our fauna at the specific and subspecific levels.

Although several references to other literature are given in the text, there is still a need for a short bibliography, which could have included some of the more useful general works on British and European Lepidoptera. No more than the usual number of minor errors seem to have arisen, but some of these lead to unfortunate confusion concerning identification; for example, on page 347 of Series 1. ab. *carthami* Herr.-Schäf. is wrongly stated to be illustrated by Fig. 11 on pl. 126.

It is disappointing to find that while this new edition is certainly an improvement on those it follows, it does not fulfil the expectations of many entomologists who had hoped for a more radical revision of the text.

A. Watson

THE GROWING TIP OF PLANTS

Apical Meristems

By Dr. F. A. L. Clowes. (Botanical Monographs, Vol. 2.) Pp. viii+217+32 plates. (Oxford: Blackwell Scientific Publications; Springfield, Ill.: Charles C. Thomas, 1961.) 37*s*. 6*d*. net.

DURING the past twenty years or so, there have been many investigations of the apical meristems of plants, an interest which is understandable since these meristems are in a sense regions of permanent embryogeny responsible in most plants for all longitudinal growth and the continued production of new organs. The early investigations of shoot and root apices were mainly anatomical, but in a considerable number of the recent investigations biochemical and experimental approaches have shed new light on the behaviour of the apical meristems. Although special

aspects of this recent work have been reviewed previously, there has hitherto been no reasonably comprehensive account of both root and shoot apical meristems. This need has now been met by the new book written by Dr. Clowes.

Although Dr. Clowes' own research work has been mainly on root apices, shoot meristems receive adequate consideration; in fact eleven of the seventeen chapters deal mainly with shoot apices. Recent work involving new techniques is discussed in some detail, but the anatomical side is not neglected. Chapters on planes of division in shoot and root apices include discussions of the tunica-corpus hypothesis of the shoot apex and of the similar, but less well-known, Körper-Kappe hypothesis of the root meristem. A complete chapter is devoted to the bearing of the evidence from chimeras on controversies relating to the shoot apex. The sections of the book dealing with the rates of cell division in both root and shoot apices are particularly informative, and it would seem that the newer techniques, including autoradiography, have demonstrated the existence of a 'quiescent' centre in the root apices investigated. It has also been shown that, in opposition to the views of the French school, there is no 'méristème d'attente' in the shoot apex.

The book is not restricted to a consideration of apical meristems in the narrow sense, but covers in addition such topics as the development of leaves, the determination of sites of leaves, the differentiation and origin of procambium, latitudinal growth in apices and the formation of floral apices. There is also a detailed consideration of differentiation in the root apex.

The text figures of apices are not very numerous, but are supplemented by 32 photographs including some striking autoradiographs of shoot and root apices. The clear readable style is an admirable feature of the book, which is a useful addition to the new series of botanical monographs. A. ALLSOPP

ELECTROLYTES AND PLANT CELLS

Electrolytes and Plant Cells

By Prof. G. E. Briggs, Dr. A. B. Hope, and Prof. R. N. Robertson. (Botanical Monographs, Vol. 1.) Pp. x+217. (Oxford: Blackwell Scientific Publications; Springfield, Ill.: Charles C. Thomas, 1961.) 40s. net.

THE stated purpose of this new series of Botanical Monographs is to inform the advanced student, assist the lecturer and be a point of departure for the specialist. The first volume admirably fulfils these aims.

Forty pages at the beginning are devoted to an account of the physical properties of electrolytes in solution. The principles of ionic exchange receive little attention, but diffusion and Donnan equilibria are dealt with handsomely. Plant cells merit no more than passing mention until Chapter 4, which contains an elementary account of the gross structure of three types. Chapter 5 deals with fine structure as revealed, albeit still imperfectly, by electron-microscopic investigations. One is left wondering how soon it will be possible to apply the physico-chemical principles outlined earlier to the immensely complex and ever-changing cytoplasm. At present only the inert cellulose wall seems amenable to such an approach.

The concept of 'free space' receives detailed consideration in Part 2. For the benefit of the uninitiated, free space may be defined as that part of a cell or tissue into and through which solutes move readily by physical processes. The authors have at various times separately suggested that cytoplasm forms part of the free space. They now conclude that it can be adequately accommodated in water-filled spaces in and around the cell wall. This is a return to the classical view—never relinquished by more conservative plant physiologists, who are unable to accept the idea of cytoplasm being freely accessible to the vicissitudes of the environment. The possibility that a small but more interesting fraction of the free space may be associated with the cytoplasm is still not excluded, but adequate evidence is lacking.

Part 3 is concerned with the active absorption of salts and its connexion with metabolism. The principles of an ion-carrier mechanism are set out, and a general scheme linking anion transport to electron flow is outlined. Cation movement is said to occur passively along an electro-chemical potential gradient established by anion movements. No explanation is offered for the active extrusion of sodium ions which occurs in some algae and in yeast. It is surprising that Conway's 'redox pump' is not mentioned in this context since it seems to differ fundamentally from the mechanism proposed only in that it is designed to transport cations rather than anions. Presumably in the authors' minds yeast is not looked on as a respectable plant cell, but surely it is unwise to confine one's attention narrowly in discussing such a fundamental biological process as ion-transport.

In a short final section, some aspects of salt absorption and transport in organs and intact vascular plants are reviewed. It is evident that adequate understanding of these processes which involve yet another level of complexity must await further knowledge of ion movements at the cellular and sub-cellular levels. JAMES F. SUTCLIFFE

ORCHIDS OF TRINIDAD AND TOBAGO

Native Orchids of Trinidad and Tobago

By Dr. Richard Evans Schultes. (International Series of Monographs on Pure and Applied Biology. Division: Botany, Vol. 3.) Pp. x+275+21 plates. (London and New York: Pergamon Press, 1960.) 100s. net.

THE third volume in the Pergamon Press's Botanical Division of its new series of Biological Monographs endeavours to maintain the standards set by the two previous volumes of Dr. Turrill and Dr. Bor on general botany and Indian grasses respectively.

Constituting the second largest plant family in Trinidad and Tobago the 180 species of Orchidaceae occurring there merit an account. The continued use of Trinidad as an exporting centre for American plants, combined with the fact that so many of its orchids are at the same time beautiful, horticulturally amenable and scientifically interesting, doubly merits an account of the colony's orchids. This was realized long ago, and Grisebach (1864), Cogniaux (1910), Broadway (1918–32) and Wilson (1925) all published accounts of the species of the area, but it has been

left to Dr. Schultes to produce this comprehensive account dealing with Trinidad and Tobago only. The classical Flora style that he adopts is admirably suited to the needs of present-day botanists, growers and collectors.

The first pages are concerned with a general treatise on the orchids followed by a historical account of collecting in Trinidad and Tobago and the subsequent research. There are dichotomous keys to all genera and species, and constant usage during the past few weeks has shown these to be as useful and accurate for determining pressed specimens as for living plants.

The main text is composed of a description of each genus followed by a specific key and the descriptions and synonymy of each species. The arrangement of genera follows that of Schlechter, which most herbaria nowadays adopt. To have the genera grouped according to their 'affinities' is obviously of great use, but, unfortunately, the arrangement of species follows the same rule as in other recent American Floras, that is, alphabetical. Affinities between species are therefore not indicated and this can be disastrous when attempting to identify species of a critical nature especially when the keys are also avowedly artificial. The species are numbered, but this is quite pointless as the numbers follow the alphabetical sequence.

Taxonomic science is a matter of opinion and no criticism should be levelled at Schultes' concepts, but nomenclature and phytogeography are more absolute sciences and it is in the interests of all that a few errors be mentioned.

The Jack Spaniard, a commonly cultivated species, is named (p. 180) as *Gongora maculata*, but this should be *G. quinquenervis*, a name published for this entity thirty-five years before *G. maculata*, as indeed the author states in his synonymy. *Stanhopea grandiflora* (p. 177) is an incorrect name as the epithet *grandiflora* was not published in Loddiges' *Botanical Cabinet*, which was just a book of coloured plates with none of the descriptions or dissections necessary for validation of the names. The correct name is *Stanhopea eburnea*, this epithet being published earlier than the validation of *grandiflora*. A much more complicated case is that of *Polystachya luteola* (p. 154), correctly *P. extinctoria* (for a full discussion of this see *Taxon*, **9**, No. 5, 150; 1960).

A more serious misleading mistake is that the term *ex* is erroneously used. Its use is reserved as a conjunction linking the authors' names when the later author published an earlier author's manuscript name. In his citation of *Maxillaria liparophylla* (p. 210) Schultes authorizes it with Summerhayes *ex* Sandwith, whereas it should be Summerhayes *in* Sandwith. Sandwith did not take up an unpublished name of Summerhayes but Summerhayes actually published the name in a general account by Sandwith.

A common misconception in the United States is perpetuated in page 162 concerning *Eulophia alta* being introduced into Africa from America. Its widespread distribution in Africa suggests that this is impossible and that this species should join the list of those common to the Old and New Worlds.

The book is typographically well produced and well printed on a white paper that does credit to the most excellent line-drawings selected from the archives of the Oakes Ames Orchid Herbarium at Harvard. Species representative of most genera are illustrated by the pens of such artists as Elmer Smith, Gordon Dillon, G. C. K. Dunsterville, Blanche Ames and many others, and although they have all appeared in previous publications this in no way distracts from their utilization here.

It is unfortunate that photographs were used so obviously as an afterthought, probably under the erroneous impression prevalent to-day that photographs boost sales. Good photographs of well-selected species probably would help the publication, but poor photographs, ill chosen (of species already amply illustrated by the line drawings) as are those in this book, increase the price but detract from the value. The photographs are of no conceivable æsthetic or scientific value whatsoever.

In all fairness the book does enable one to achieve the prime object of a Flora—to identify plants ; but just a little more care and thought would have rendered it so much more useful.

P. Francis Hunt

ECOLOGICAL BRANCH OF RUSSIAN PARASITOLOGY

Parasitology of Fishes

By V. A. Dogiel, G. K. Petrushevski and Yu. I. Polyanski. Translated by Dr. Z. Kabata. Pp. x+384. (Edinburgh and London: Oliver and Boyd, Ltd., 1961.) 84*s*. net.

THIS book was inspired by the wish of Valentin Alexandrovich Dogiel to institute collective discussion of theoretical and practical problems involved in the parasitology of fishes. Wearied by lists and descriptions of new species, he yearned for knowledge about the whole life of the parasitic fauna which he foresaw as a weapon in the fight against parasitic diseases. In 1927 he founded this ecological branch of Soviet parasitology and in 1930 the parasites of fishes became a priority study. The vast territory of the U.S.S.R. comprises most of the habitats of fishes which exist on the Earth, and ultimately all the main rivers, most of the large lakes and both internal and bordering seas were being examined in great parasitological detail. He wrote the first chapter of this book himself, and most of the others were written with his guidance. Regrettably, he died on June 1, 1955, but in 1958 his wish was to some extent fulfilled when the Russian original of this book was published.

Dogiel recognized the prime peculiarity of the parasite, that its environment is furnished by another living organism, the host. I do not believe that his choice of fishes as hosts was accidental, because this is the most ancient class of the vertebrates and it harbours more parasites than does any other class. Moreover, fishes are important in relation to food supply, and in this book we can recognize a great urge to implement research for economic reasons. Dogiel's study of the dynamics of assemblages of parasites inhabiting one host ('parasitocœnoses') convinced him that the environment of the parasite comprises the host (the micro-environment) and the habitat of the host (the macro-environment). The composition of the parasitic fauna of fishes depends on changes in the habitat of the host and changes in the physiological states of the host. Geographical location, the season of the year, characteristics of water and bottom in rivers, lakes and the sea, related organisms in and around the habitat, and many other biotic and abiotic features of the environment provide the means of life for host and parasites alike. The

composition of the parasitic fauna is determined also by the nature of the food and digestive equipment of the host, and other influential factors are age, general condition as indicated by states of nutrition or inanition, times of spawning, migration, hibernation and even speeds of locomotion. The nature of the integument of the host and its secretions influence parasites which penetrate the skin, some of which are parasites of man. Many patterns of correlated environmental factors fluctuate periodically and modify the composition of the parasitic fauna.

Dogiel's influence is seen in various chapters of the book dealing with such topics as the ecology of parasites of marine and freshwater fishes, questions concerning host-parasite relationships, specificity, life-cycles and zoogeography. Some consideration is given to the parasites of fishes living in reservoirs, changes in the parasitic fauna of acclimatized fishes, parasitic diseases of fishes living in natural waters and also cultured fishes, and fishes as transmitters of human helminthic disease. The parasites considered are mainly Protozoa, Platyhelminthes, Nematoda, Acanthocephala and Copepoda. Many isolated observations provide interesting revelations but extensive regional surveys may give the specialist more satisfaction. The format is pleasing, the translation is readable, and the text is illustrated with diagrams and maps and supplemented by comprehensive tables. More than 700 references to the original literature are cited, nearly two-thirds of them from the Russian. Errors are few and mainly typographical but sometimes surprising: the statement on p. 105, "Monogenoideans with a single host", refers to several digenetic trematodes but no monogenetic forms.

Students and teachers will find in the book a fund of readily assimilable information, and if the appetite of the specialist is sometimes unsatisfied the gaps more often than not indicate the opportunities for research workers in the future. All concerned with the production of the book deserve credit for giving biologists this opportunity to evaluate Russian progress in a branch of parasitology which has been neglected in Britain. BEN DAWES

SALT MARSHES AND SALT DESERTS

Salt Marshes and Salt Deserts of the World

By Prof. V. J. Chapman. (Plant Science Monographs.) Pp. xvi + 392 + 45 plates. (London: Leonard Hill (Books), Ltd.; New York: Interscience Publishers, Inc., 1960.) 95*s*. net.

LET the good things be placed on record first. This book brings together a wealth of information from widely scattered and often inaccessible sources and illuminates it with the author's own long experience of salt marshes. Any student undertaking work in this field in the future will certainly start by "looking it up in Chapman". For this service all botanists will be grateful; but gratitude need not blind us to the book's many faults, nor will it arm the struggling reader against exasperation. For the book is, frankly, not so much written as thrown together.

It opens inauspiciously with a chapter which hovers uneasily between a statement of intentions and a summary of findings. This is followed by three chapters on general features of the habitat, the chief fault of which is that they are insufficiently general; all too often a promising principle collapses into a detailed study of a specific example. In the next five chapters we are taken on a conducted tour of the salt marshes of the world, and here the author is at his best; we realize that information about the different areas will be uneven, and presentation of these scattered and largely unrelated data is congenial to the author's discursive style. Elaborate and detailed successional schemes are, however, given with an off-hand confidence which is likely to arouse misgivings. Finally, there are three miscellaneous chapters. The first of these summarizes the author's own views on the successions and phytosociological entities represented, and these are most welcome; but the chapter continues with a quantitative study of the affinities between communities which suggests that the author is unaware of the difficulties in devising and interpreting parameters suitable for this type of comparison. The chapter ends, unaccountably, with a brief account of salt-marsh fucoids. Then follows a disastrous chapter on "Physiology of Halophytes", in which the whole of the thinking concerning transpiration is out of date, and the statements concerning ion uptake simply fail to make sense. The book ends with a brief but interesting account of economic uses.

It is all clearly the work of a man passionately devoted to his subject, avidly and uncritically welcoming any scrap of information which comes his way, but still too involved in minutiæ to discern underlying patterns. If Prof. Chapman, secure in his remarkable knowledge, had brooded over his information for a year or two, and then written, and re-written, and revised, he might have given us a new classic; as it is, botanists can only weep for what might have been and go and buy the book. W. T. WILLIAMS

MICROSCOPY IN A MAZE

The Encyclopedia of Microscopy

Edited by Prof. George L. Clark. Pp. xiii + 693. (New York: Reinhold Publishing Corporation; London: Chapman and Hall, Ltd., 1961.) 200*s*. net.

THIS is not an encyclopædia in the ordinary sense, but a collection of 140 articles. There is no index, and the subject titles are not always helpful. It is thus very difficult to look up any specific point. The articles are strung together with little correlation or cross-reference, leading to useless repetition or omission of important topics. The two articles on interference microscopy cover much common ground and contain several similar diagrams, but no adequate discussion of phase contrast is to be found. There is a good article on the design of the polarizing microscope for detecting very weak birefringence, but no proper description of the basic instrument or its use in crystallography. Fluorescence microscopy is represented by two pages from a commercial brochure. Fluorescence labelling of proteins, which has led to one of the most important advances in modern biological microscopy, is not mentioned.

The section on ultra-violet microscopy contains three pages on methods, with almost no discussion of results or applications, one page on colour translating television systems (with no references) and more than nine pages on "Image Formation by a Fresnel Zone Plate". The latter article might find a place as an original paper in a specialist journal; but why

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it was given so much space when so little was devoted to ultra-violet microscopy itself is a complete mystery.

This lack of balance and bad choice of material is seen throughout the book. There is virtually no discussion of resolving power, no description of light sources, no section on photomicrography, yet 30 pages are devoted to non-microscopic refractometry. This section is remarkable, for although it includes descriptions of many refractometers and interferometers, it contains not a single diagram of any sort. Electron microscopy is equally unbalanced. Biological microscopy has been revolutionized by new methods of fixation, embedding and ultra-thin sectioning, but the article on specimen preparation deals only with special non-biological methods used at Los Alamos. Such an omission can only be described as fantastic.

The choice of biological subjects is quite extraordinary. Thirteen pages are devoted to "kidney ultrastructure", but this is the only organ dealt with. Why kidney ? Why not liver, glands, digestive or nervous systems, for example ? One turns to the heading "Pathology" in the hope of reading a much-needed general article on the use of electron microscopy in this field, only to find that another thirteen pages are devoted entirely to the kidney. Unfortunately, one could go on writing in this vein for quite a long time. Any book of 700 pages is likely to contain some useful information; but it is a pity to see so much effort wasted by bad editing and poor selection of material.

R. Barer

STUDIES IN ENDOCRINOLOGY

Études d'Endocrino'ogie

Séminaires 1960 de la Chaire de Morphologie Experimentale et Endocrinologie du Collège de France dirigés par le Professeur Robert Courrier. (Actualités Scientifiques et Industrielles, No. 1286.) Pp. xiv + 350. (Paris: Hermann, 1961.) n.p.

SINCE 1959 some of the advanced courses of lectures which it has long been the tradition for professors of the Collège de France to deliver have been replaced by public seminars at which eminent research workers are invited to discuss the results of their studies. The records of two such occasions, both arranged by the Department of Experimental Morphology and Endocrinology, have now appeared.

The first deals with the gonadotrophins, and was organized jointly by Prof. Robert Courrier and Dr. Marian Jutisz. The published proceedings provide an up-to-date account of the various gonad-stimulating hormones which can be extracted from pituitary tissue, from the urine of pregnant women, from human urine after the menopause, and from the blood serum of pregnant mares. An account is also given of the relationship of sheep pituitary prolactin to other gonadotrophins. The papers which describe these various hormonal substances are published in full, with a record of the discussion which followed each day's presentation. Four general papers concluded the seminar, and each raises some issue of wide importance. The first, by Prof. Max Aron, takes up the much-debated question of the degree to which, both qualitatively and quantitatively, luteinizing and follicle-stimulating hormones are distinct hormones. The experiments on the guinea pig which he reports tend to indicate that as entities they are not as separate as is usually taught. Dr. Robert Henry's contribution on the biological dosage of hypophysial gonadotrophins leads to a contrary view, however, with respect to follicle-stimulating hormone and interstitial cell-stimulating hormone; and the paper by Dr. Pierre Aschheim—the son of the Aschheim whose name is associated with that of Zondek in the discovery of human chorionic gonadotrophin—also supports the view of the separate chemical identity of various gonadotrophins. In the general discussion following the presentation of these papers, follicle-stimulating hormone, interstitial cell-stimulating hormone, the post-menopausal urinary gonadotrophin of women as well as pregnant mare serum were, none the less, set aside as substances which had not yet been isolated in a state of sufficient purity to be regarded as chemically separate. Human chorionic gonadotrophin and prolactin, on the other hand, seem to satisfy the criteria of chemical purity, although it was made plain that the criteria of purity are themselves arbitrary.

The broad conclusion which emerges from the whole discussion is that much more work will need to be done before we can expect to understand the underlying chemistry of the reactions of the ovaries and testes to the numerous gonadotrophic preparations which the biochemist has already isolated. Of facts about gonadotrophins we have plenty; what we lack is an underlying hypothesis which strings them together.

The second part of the volume records a seminar arranged by Dr. Roger Guillemin on the functional relations of the hypothalamus to the adenohypophysis, with particular reference to the release of adrenocorticotrophic hormone. In this field of research the facts, while also numerous, seem somewhat more untidy than those which were dealt with in the first seminar—while of hypotheses there is not a single one which is not characterized more by empty speculation than by predictive value.

The opening paper in this symposium was by Prof. André Delmas, and dealt with the anatomy of the hypothalamus and its connexions. Prof. Delmas was followed by Dr. Henri Duvernoy, who reported a series of observations on the vascular connexions between the adenohypophysis, the neurohypophysis and the median eminence. Contrary to the fashionable belief that has been so assiduously disseminated in recent years, it is now clear that the vascular system of the anterior pituitary connects freely not only with the pituitary portal vessels, but also with the vessels of the neurohypophysis and, through the portal vessels, with those of the hypothalamus. This observation is a further nail in the coffin of the theory, based on 'negative' observations, that the pituitary portal vessels form a unique connexion between the hypothalamus and the anterior pituitary, and that through them passes some chemical mediator of hypothalamic origin which stimulates the anterior pituitary to release its various hormones as demanded by the physiological state of the body. Dr. Duvernoy's new data make it plain that any chemical mediators which the hypothalamus might produce and which enter the pituitary portal vessels could reach the posterior pituitary as well as the anterior pituitary: and if any local hormonal action were involved in the control of the anterior pituitary, there is no reason for supposing that there is any physical barrier to the passage of substances in whatever direction one cares to suppose. But all this is pure speculation.

The second symposium also dealt with the technique of measuring changes in the level of secretion and action of adrenocorticotrophic hormone, as well

as with the variety of nervous stimulations which leads to the discharge of adrenocorticotrophic hormone. The evidence in favour of the alternative views that the release of adrenocorticotrophic hormone is mediated by some neurohumoral substance of unknown chemical nature (the so-called CRF) or by vasopressin, or by melanophore-stimulating hormone, was reviewed by Dr. Guillemin, but there seems little that is precise about these matters, and as the general discussion at the end of the seminar indicated, considerable doubt exists about the assumed localization of hypothalamic function with respect to the control of pituitary function.

The verbatim record of what passes at endocrinological symposia has on occasion detracted from the value of what might otherwise have been regarded as scientific meetings of high quality. On this occasion this is not so. Not only do the papers which were delivered at the seminars of the Collège de France provide a first-rate account of the matters with which they deal, but it is also plain from the record of the discussions that Prof. Courrier kept the several sessions of the two seminars very much to the point. He is to be congratulated for having inaugurated a series of seminars which will, one is certain, continue to enjoy the high standard of the two now published.

S. ZUCKERMAN

HÆMOGLOBIN: NORMAL AND ABNORMAL

Hemaglobin and Its Abnormalities

By Prof. Vernon M. Ingram. (A Monograph in American Lectures in Living Chemistry.) Pp. xiv+153. (Springfield, Ill.: Charles C. Thomas; Oxford: Blackwell Scientific Publications, 1961.) 60*s*.

HÆMOGLOBIN is the most intensively studied of proteins. Many of the techniques available to the physiologist, biochemist, biophysicist and geneticist have at one time or another been applied to hæmoglobin. All this work has led to spectacular progress in our understanding of the structure and function of hæmoglobin and its near relative, myoglobin.

Last year saw the publication of papers that represent the culmination of long and detailed analysis by the investigators concerned. Kendrew and his colleagues have extended the resolution of data from their X-ray diffraction patterns of myoglobin to the 2 Å.-level, so that for the first time the helical arrangement in the polypeptide chain of a protein can be unequivocally demonstrated. At the same time, Perutz *et al.* published the structure of hæmoglobin at a resolution of 5·5 Å. Because of its very great similarity to the myoglobin structure, they have been able to infer considerably more than the actual resolution allows. From these X-ray diffraction patterns detailed information about the secondary and tertiary structure of proteins in crystalline form can be deduced. There is already correlation of structures deduced from X-ray patterns with the amino-acid sequences which are now known for the human hæmoglobin chains and nearly all known for horse hæmoglobin chains and myoglobin.

In 1949, Pauling *et al.* demonstrated that the basic defect in sickle-cell disease is an abnormal hæmoglobin. The term 'molecular disease' introduced by Pauling for conditions of this kind has caught the imagination of many research workers and provided a great stimulus to research in the field. Eight years later Ingram applied Sanger's technique of peptide analysis to normal adult and sickle-cell hæmoglobins. He found that the two molecules differ only in a single peptide, and later this difference was shown to be due to the substitution of the amino-acid valine for glutamic acid which occupies the sixth position from the amino-terminus of the β-polypeptide chain of the normal molecule. Ingram and his co-workers, and later others, have shown that several other abnormal hæmoglobins differ from the normal by single amino-acid substitutions in the β- or α-chain. There was formal evidence that genes controlling the synthesis of normal and abnormal β-chains were allelic with one another but not with genes controlling synthesis of α-chains.

Ingram's important discovery could not have come at a more opportune time. The importance of proteins in mediating genetic effects transmitted by nucleic acid had emerged from the publications of Crick and others, and there was a great need to know the sort of effects on protein structure produced by mutation of the genes controlling their synthesis. The studies of Ingram and his colleagues provided precisely the required information. The technique of peptide analysis, re-named by Ingram 'fingerprinting', came to be used in many laboratories for establishing exact structural differences between related proteins.

In the book under review Ingram gives a general account of these developments, beginning with the structure and function of the normal hæmoglobin molecule and describing the structural differences in some of the known abnormal molecules. The arguments are well presented and easy to read. There are few mistakes (in caption 2 to Fig. 46 *S* should be replaced by *F*). Diagrams and references have been carefully selected and provide an excellent introduction to the field. So much has been done that it is, of course, impossible to expect a book of this length to serve as a comprehensive reference work. Although the main emphasis of the book is biochemical, the diseases associated with the abnormal hæmoglobins are briefly discussed and a few of the interesting problems in population genetics raised by the high frequency of certain abnormal hæmoglobin genes in some human populations are mentioned. In connexion with the latter, Ingram quotes the extraordinary and unfounded suggestion that "hæmoglobin E might have a selective advantage because in the presence of this gene the likelihood of an allelic thalassæmia disease occurring in homozygous form is removed".

This book is likely to be read by many people with an interest in biochemistry and genetics, and it seems a pity that, although only 150 pages long, it should cost £3.

A. C. ALLISON

ADVANCED ORGANIC CHEMISTRY

Advanced Organic Chemistry

By Prof. G. W. Wheland. Third edition. Pp. xi+871. (New York and London: John Wiley and Sons, Inc., 1960.) 17.50 dollars; 140*s*.

THIS book constitutes an extended, revised edition of Prof. G. W. Wheland's well-known book, *Theoretical Organic Chemistry*, which, for more than a decade, has been of such considerable value to

both university students and lecturers. The new edition has been well produced with most legible printing on good quality paper and the spatial and conventional organic chemistry formulations are reproduced with considerable clarity.

The historical approach employed throughout the text is thought-stimulating and interesting, the earlier chapters dealing with the general theories of valency bonding, inter-atomic force theories, etc. Electrostatic, covalent, semipolar double bond systems, etc., are clearly described, together with valuable excursions into the fields of dipole–dipole interactions, solvated chains, polarization and orientation phenomena. The first chapter, on valency and configuration, forms a natural precursor to discussions on the determination of structure by various physical methods, and general comment is made on the application of nuclear magnetic resonance, rotatory dispersion and parachor applications.

Other chapters deal with the Lowry–Brønsted theory of acids and bases, and the allied Lewis concept; a survey is made of clathrate inclusion compounds, of nucleophilic displacements, S_N and their relation to $S_{N}1$ kinetics and to $S_{N}2$ reactions of the Walden inversion type.

A most extensive chapter deals with the stereochemistry of carbon, which is well illustrated with numerous examples illustrating resolution, solvent effects, configuration studies, optical phenomena, etc. This is supplemented by a further chapter on stereochemistry of elements other than carbon, notably those of nitrogen and sulphur. Free radical chemistry also receives the most detailed treatment.

The Baeyer strain theory, steric hindrance and conformational analysis receive much attention. A memorandum by Prof. F. W. Westheimer on electrostatic affects in organic chemistry forms the basis of Chapter 11, which concludes with a rather abbreviated discussion of the Hammett rho-sigma relations. References are, however, given to H. H. Jaffe's excellent review of this quantitative empirical relation between the rate or equilibrium constants of reactions involving organic compounds. The value of kinetic data is frequently stressed throughout the book, and in all chapters the mathematical treatment is of reasonably simple character and will not prove over-burdensome to those who find the more abstruse mathematical concepts somewhat difficult to follow.

This book is an able successor to its authoritative predecessors, and will do much to stimulate original thought and constructive discussion in the ever-extending and complex field of theoretical organic chemistry.

D. T. Lewis

TEXT-BOOK OF INORGANIC CHEMICAL ANALYSIS

Quantitative Inorganic Analysis

By Prof. R. Belcher and Dr. A. J. Nutten. Second edition. Pp. x+390. (London: Butterworths Scientific Publications, 1960.) 35*s*.

It is highly commendable that the authors have so thoroughly revised a text-book that is only six years old. Among the novel features introduced are choice of appropriate redox indicators for particular systems, and criticism of uncertainties involved in the dichromate–ferrous reaction. It is a pleasure to see classical gravimetric analysis treated with due respect and yet a pity to miss a reference, presumably due to shortage of space, to the solvent extraction technique.

The reviewer disagrees with the condemnation of the swinging-point balance. In its simplicity and versatility, especially as regards control of sensitivity, it ought to remain for a long time a basic instrument in the hands of a chemist. Some minor criticisms may be mentioned briefly. Cleaning of pipettes by immersing overnight in a dichromate–sulphuric acid mixture is in the long run detrimental to the pipette inscription. On p. 150, it is pointed out categorically that laboratory glassware should on no account be warmed which, without defining temperature limits or stating reasons, sounds very dogmatic. On the other hand, the temperature control in a drying oven to within ± 1° C. (p. 10) seems exceptionally good for an average student drying oven. In the volumetric section, the conventional ferric alum is recommended as indicator in Volhard's method, while in the colorimetric section the authors state that sulphate ions tend to form complexes with iron(III). Why not propose ferric nitrate as indicator in the first instance ?

The book has been edited with great care and the occurrence of misprints such as that in the legend to Fig. 40 is exceptional.

This clear, concise, and up-to-date text-book can be whole-heartedly recommended for use by students and practising chemists.

G. Kakabadse

THE POLYNUCLEOTIDE FIELD

Polynucleotides

Natural and Synthetic Nucleic Acids. By Robert F. Steiner and Roland F. Beers, Jr. Pp. viii+404. (Amsterdam: Elsevier Publishing Company; London: D. Van Nostrand Company, Ltd., 1961.) 85*s*.

In the introductory chapter of this monograph, the authors point out that the nucleic acid and associated fields have expanded at such a remarkable rate in the post-war years that it is no longer possible to attempt a complete coverage of them in a single text. They go on to list a few of the main subdivisions such as chemical genetics, virus biochemistry, protein synthesis, polynucleotide synthesis and the physical chemistry of polynucleotides. The extensive developments in the last two subdivisions in the five-year period ending 1960 have prompted Dr. Steiner and Dr. Beers to write this book. In the final chapter they touch on some of the other main subdivisions by discussing the biological roles of nucleic acids.

The introduction, which indicates the scope of the book, is followed by a chapter on the organic chemistry of nucleotides. Then the chemical and enzymatic evidence for the nature of the inter-nucleotide linkages in ribonucleic acid, deoxyribonucleic acid and synthetic polynucleotides is discussed. This is followed by two chapters on nucleotide-polymerizing enzymes. In the first, a description of the procedures for isolating and assaying these enzymes is given, and in the second, the properties of the different enzymes are discussed. The next three chapters deal with some physical methods such as ultra-violet spectroscopy, optical rotation and X-ray diffraction, and their application to the determination of the macro-molecular configuration of natural and synthetic polynucleotides. The final chapter, mentioned above, is preceded by a discussion of the helix-coil

transition and the binding properties of polynucleotides. Besides the main text are included some seventeen appendixes which outline the experimental procedures for the isolation of nucleic acids and the analysis of their degradation products, and for the preparation, assay and use of some nucleotide-polymerizing enzymes.

The authors are certainly justified in writing a book on a subdivision of the nucleic acid field as no one or two people could possibly review every aspect of the subject critically. Such is the scope of this book that, if anything, they have tried to cope with too much for two people, although it is certainly very useful for workers in the polynucleotide field to have all this material collected in one volume. For the latter reason, Dr. Steiner and Dr. Beers are to be thanked for sorting out such a vast amount of the present-day literature.

However, it might have been wiser for the authors to have co-opted specialists to write the chemical chapter in the beginning of the book and help with the accounts of some of the other areas to which they themselves do not appear to have contributed. I would single out the chapter on the chemistry of the nucleotides for the greatest criticism. This contains formula, chemical, and factual errors and some important omissions, but it is nevertheless an adequate account of this aspect. Perhaps the only other adverse criticism of this very useful book is that it is not always written in a clear and concise style. The appendixes are a good idea and should be useful. The printing and layout are good with the exception of some of the chemical formulæ. On the whole, this book can be recommended as being of considerable value to workers in the polynucleotide field, for whom it is designed, and to other people interested in this important subject. C. B. REESE

TECHNOLOGY OF ETHYLENE POLYMERS

Polythene

The Technology and Uses of Ethylene Polymers. Edited by A. Renfrew and Philip Morgan. Second edition. Pp. xxi+781+93 plates. (London : Iliffe and Sons, Ltd. ; New York : Interscience Publishers, Inc., 1960.) 165*s*. net.

THE growth of polythene production has been one of the major features of the plastics industry in recent years. The interest aroused by the development of newer types of polythene and the many recent technological developments in the field of ethylene polymers have necessitated a considerable revision of the text of this well-known book. The present edition—the second—contains approximately 300 more pages than the previous one ; chapters have been so revised that the original text has been largely re-written in order to bring the book in line with rapid developments, particularly in relation to materials of higher density. In fact, it has been so changed and enlarged that it may be regarded as virtually a new book.

The most important additions are as follows : The chapter "Manufacturing Processes" now appears as four contributions describing high-pressure, Zeigler, Phillips, and Standard Oil Co. polymerization processes ; the chapter on the theory and mechanism of ethylene polymerization now becomes two chapters to cover, respectively, polymerization by free radicals and by ionic growth. Additional chapters are "Ethylene Copolymers and Polymer Blends", "Vacuum Forming", "Reprocessing" and two chapters on packaging which describe those varied and useful applications not classified as films. Valuable appendixes are a table of world manufacturers of polythene and their production capacities, and a list of world proprietary names for ethylene polymers.

The thirty-six chapters of this book deal with every aspect of polythene, its manufacture and properties (structure, mechanical, electrical, chemical, testing, radiation treatment, and modification) ; processing techniques (compounding, pigmentation, extrusion as applied to extruder design, cable covering, tube, rod and profile, film and sheet, injection and blow moulding, centrifugal cast, coating and laminating, dip and spray coating, vacuum forming and reprocessing), and applications (cables, film, coated packaging products, pipes, chemical plant, household goods, textile yarns and fibres). Each of the chapters, written by an expert either from Europe or the United States, provides a most complete and authoritative account of the technology and uses of this important polymer. The book remains the standard work on the subject. C. E. H. BAWN

GAS DYNAMICS IN THE U.S.S.R.

Physical Gas Dynamics

Edited by A. S. Predvoditelev. Translated from the Russian by Dr. R. C. Murray and D. R. H. Phillips. Pp. v+183. (London and New York: Pergamon Press, 1961.) 50*s*. net.

THIS book is a translation from the Russian of a symposium of twelve papers covering a wide range of topics under the general heading of the title.

Five of the papers cover the field of gas kinetics, the longest being concerned with calculating the properties of air in the temperature-range 1,000° K.–12,000° K., and the pressure-range 0·001–1,000 atmospheres. Two of the other papers calculate the changes across normal shock-waves in air considered as a real gas.

The next two papers consider experimentally the supersonic flow at an oblique-cut nozzle and an oblique-cut base. These are related to the flow in turbine nozzles and blades.

The next three papers again present a sharp contrast, the subject under discussion being the pressure field resulting from electrical discharges under water, while the last two papers in the book discuss shock waves associated with flames. Four of these five papers discuss experimental work.

One of the difficulties encountered by publishers of a book of this nature is that of making the information available sufficiently quickly after completion of the work on which it is based. The references to the various papers indicate that most of the work presented at the symposium was done prior to about 1956, so in this sense the book is not up to date; but, despite this, there is no doubt that it gives some of the most up-to-date information in English on the work being carried out in the U.S.S.R. in the field of gas dynamics.

It is fair to say that the translation into technical English is in general excellent, though it is noted that in some references which were originally in English, but have been translated into Russian, the authors' names are not correctly translated back into English. The printing is in non-letterpress type

setting, but this in no way detracts from the book, perhaps the only thing which does being the quality of schlieren photographs on which several of the papers depend. The photographs are in general poor, but there is no indication whether this is due to the printing process used or to the poor quality of the originals.

I. S. Donaldson

SURVEY OF ASTRONOMY

Vistas in Astronomy

Edited by Arthur Beer. Vol. 3, Part 1: Dynamics—Geophysics—Instruments—Solar System. Vol. 3, Part 2: Stellar Astronomy—Stellar Evolution—Photometry—Galaxies—Spectroscopy—Cosmology. (Special Supplement No. 7 to the *Journal of Atmospheric and Terrestrial Physics*.) Pp. vii+345. (London and New York: Pergamon Press, 1960.) 120*s*. net.

THE third volume of *Vistas in Astronomy*, published, as in the case of the two preceding volumes, by Arthur Beer, opens with an article by R. van der R. Woolley, Astronomer Royal, on "The Dynamics of Stars in the Neighbourhood of the Sun". The author deals in particular with the movements of stars near at hand, the permanence of very open clusters and the equipartition of energy. R. A. Lyttleton poses the following question: "What is the simplest theoretical approach and minimum amount of calculation that could have led to the discovery of the planet Neptune?" Tisserand had already posed this question in his *Mécanique Céleste*, when he suggested that it would suffice to assign successive values to the radius of the planet, which is supposed to have a circular orbit. Lyttleton shows that one can simplify the problem considerably without altering the numerical solution much, by attributing circular orbits to both Uranus and Neptune. The position which he finds for the hypothetical planet does not differ more than one degree from the observed position; as for its mass, he approximates the real value more closely than Adams and Le Verrier. But he has the advantage over his two predecessors of knowing that Neptune exists, whereas in 1845 or 1846 it was doubtful, as the question posed by Airy to Adams at first and then to Le Verrier proves. What is more, we know that the orbit of Neptune has a slight eccentricity. The paths of discovery are often tortuous, but one does not perceive this until the goal has been attained.

The contribution of H. von Klüber is also of great interest and of more immediate application. It is a discussion which takes into account all the determinations, made since 1919, of the displacement of stars around the Sun when in eclipse. The existence of this effect is not in question, but the extent of displacement remains very uncertain. It appears, however, to be greater than that provided by theory. The observations are very scattered and, in consequence, the hyperbolical variation of the displacement as a function of the distance from the Sun cannot be considered as established. The recommendations directed by H. von Klüber to future observers must be acclaimed without reserve.

Of interest are articles, one by W. Cochran, the other by V. Fock, on "The Clock Paradox"; some studies by G. M. Sisson on the "Design of Large Telescopes", by Marschal A. Wrubel on "The Electronic Computer as an Astronomical Instrument", by A. H. Jarrett on "Techniques in Auroral Investigations" and by D. W. Beggs on "The Russian Satellites". Finally, four notes on the brilliant comets of 1957 complete the first part of this volume.

John B. Irwin opens the second part with an article entitled "The First 70,000". It is the exposition of a vast programme of observations destined to yield the following for all stars down to magnitude 8·5: position, proper motion, magnitude, multicolours, spectral type, luminosity, parallax, radial velocity and polarization. The author emphasizes, by an apt title, the paucity of information we have on the southern hemisphere. He discusses the use of the transit circle for the determination of positions and proper motions, but he does not mention the use of the impersonal astrolabe for establishing the fundamental catalogue. Altogether, the programme outlined by John B. Irwin is excellent, but only international co-operation will allow it to be executed. It would be an interesting task for the International Astronomical Union.

Modern aspects of stellar photometry are dealt with in two articles, one by Gerald E. Kron on "Multiple Colour Photometry", the other by A. N. Argue entitled "Photometry with the Cambridge Schmidt Telescope". A long study by B. E. J. Pagel provides interesting ideas on "The Excitation of Emission Lines in the Spectra of Early-type Stars".

Olin J. Eggen has prefaced his article, "Colour, Luminosity and Evolution of the Stars", with some opinions of this evolution by celebrated men of science, from Helmholtz (1854) to Eddington (1926). This comparison of ideas put forward by very high authorities produces an effect of shock on the reader of to-day and inspires him to salutary reflexions on what H. Poincaré called "La Valeur de la Science". Eggen shows, with diverse examples, all that photometry of stellar clusters in several colours teaches us about stellar evolution. The volume ends with a representation of "The Visual Milky Way" by Sergei Gaposchkin and with two theoretical studies, one by L. Mestel entitled "Star Formation and the Galactic Magnetic Field" and another by D. W. Sciama called "Observational Aspects of Cosmology".

Presented with the same care as the two preceding ones, Volume 3 of *Vistas in Astronomy* contains an abundant bibliography and a very detailed "Name and Subject Index"; it is an excellent piece of work. The editor announces the publication of two other volumes, the authors of which will be drawn from fifteen countries or so. *Vistas in Astronomy* is indeed of immense utility for all those who wish to know the state of advancement of the diverse branches of astronomy.

A. Danjon

THE NATURAL HISTORY OF GALAXIES

The Hubble Atlas of Galaxies

By Allan Sandage. Pp. viii+32+50 plates. (Washington, D.C.: Carnegie Institution of Washington, 1961.) 10 dollars.

THIS is a remarkable and fascinating book. Conceived by Edwin Hubble, who did not live to see it finished, and now completed by Hubble's pupil and successor, Dr. Allan Sandage, it can be recommended to a very wide range of readers, from

mature specialists in cosmology to young people with a good sense of curiosity and wonder. It consists of reproductions of photographs of 176 galaxies, taken almost entirely with the large reflectors of the Mount Wilson and Palomar Observatories, and many made by Hubble himself. The photographs are of the highest technical quality and are unlikely to be surpassed until we learn to build much better telescopes, or invent new techniques, perhaps involving artificial satellites. Although reproduction is by a half-tone process, such care has been taken that one can often see detail down to about 1 second of arc in diameter. In a number of cases two, or even three, prints are given, since the range of surface brightness is too great for one print to show all structure of interest.

A preface describes the origin of the *Atlas* and this is followed by a chapter entitled "Galaxies", giving a summary of immediately relevant information, including some very instructive, and sometimes amusing, history that ought to be compulsory reading for all astronomers. This is followed by a long and detailed description of Hubble's system of classification, which the *Atlas* was designed to illustrate, with frequent references to individual photographs. Besides this, each photograph is provided with its own commentary, usually about 100 words but sometimes considerably more.

If we exclude clusters of galaxies and the universe itself, galaxies are the largest physical structures known to man. We believe them all to be aggregates of gas, dust and stars, of total masses mostly in the range 10^9–10^{11} Suns, and with rather ill-defined optical diameters of the order of 10^4–10^5 or more light years. Hubble's system of classification, the simplest proposed so far and perhaps for most purposes the most useful, is a purely morphological one. The outstanding characteristic of nearly all these objects is that their form strongly suggests rotation, and spectroscopic measurements confirm this. Hubble arranged galaxies into an order which in general is one of increased flattening, increased development of spiral arms, diminishing nucleus, growing signs of interstellar dust, probably more interstellar gas, more resolution into stars and greater abundance of young, hot stars. He was always careful to point out that his sequence is not necessarily one of evolution, in either direction. Sandage follows him, but can add in the light of more recent work that, whether evolutionary or not, the sequence as just described appears to run from old to young.

One criticism of Hubble's scheme has been that it may impose too simple an order on an essentially complicated problem. For other reasons too, having little to do with Hubble, most astronomers until fairly recently have tended to carry in their minds an altogether too regular and standardized picture of galaxies. Fortunately, a better appreciation of the problem has been growing and now this *Atlas* makes it abundantly clear that galaxies, like most natural objects, are very far indeed from being simple, mass-produced structures. Most of our respectable old friends are here, for example, *M*31, *M*33, *M*81, but so also are some much more awkward customers. What of *NGC*520, 2685, 2859, 5128, or even the Large Magellanic Cloud? What are we to make of the nuclei of four *Sc* spirals, here reproduced separately on a large scale, on page 31?

Hubble's original scheme, apart from a bifurcation between ordinary and barred spirals, is essentially one-dimensional. But even on a purely morphological basis the quite limited sample of galaxies here cannot be fitted in neatly without qualification. As Sandage remarks, "the classification sequence is not infinitely narrow perpendicular to the $Sa \rightarrow Sb \rightarrow Sc$ direction". Among *Sb* spirals, for example, he directs attention to variations in the size of the nucleus, in the thickness and surface brightness of the arms, and in the distribution of dust. Some *Sb* galaxies have two sets of arms, of different pitch. Among the *Sc* galaxies "at least six major sub-groups can be distinguished". Nevertheless, as a broad generality, a first approximation, Hubble's scheme still impresses one as valid.

Although a mine of information, *The Hubble Atlas of Galaxies* is not a text-book. Possibly the author should have emphasized this more in his preface. It makes no pretence of dealing with the general problems of galaxies, of their dynamical structure, of their physical composition as revealed by the spectroscope, of their motions, of pairs of galaxies, multiple galaxies, colliding galaxies, linked galaxies, clusters of galaxies. There is nothing of radio-astronomy, its results and its perplexities.

There is also no discussion of the technical problems of photographing galaxies, the outer parts of which are much fainter than the natural sky background itself. (In these pictures the sky is reproduced nearly perfectly black; æsthetically satisfying but scientifically a little misleading.) We are limited not by photographic speed but by sky brightness. Equally, we cannot photograph detail less than about one second of arc, not because of the imperfections of telescopes and photographic emulsions, or their limited resolving power, but because of the optical irregularities of the Earth's atmosphere. I think all this needs to be said clearly. Observational astronomers take these familiar limitations for granted, but they are imperfectly understood by many others who may be users of this volume.

What it comes to, of course, is that we need a full text-book on galaxies to accompany the *Atlas*. Could Dr. Sandage provide such a companion volume to give us instruction and pleasure in the same generous measure as does the *Atlas* itself?

R. O. REDMAN

THE HIDDEN FACE OF THE MOON

Atlas of the Other Side of the Moon

Edited by N. P. Barabashov, A. A. Mikhailov and Yu. N. Lipskiy. Translated into English by Leon Ter-Oganian. First published by the Academy of Sciences of the U.S.S.R. Pp. 141 + 30 photographs. (London and New York: Pergamon Press, 1961.) 50*s*.

EVERYONE is familiar with the fact that the tidal friction operative in the Earth–Moon system has gradually slowed down the axial rotation of our satellite to the rate with which it revolves around Earth (the periods of these two motions being now synchronized within at least 0·1 sec.)—which makes the Moon show us always the same face. Lunar librations (both physical and optical) permit us, to be sure, to see from Earth somewhat more than one-half of the entire surface of the lunar globe—in fact, about 59 per cent of it—but the rest remained completely hidden to us, until the memorable flight of the third Russian space rocket in October 1959, which circumnavigated our satellite and by means

of its photographic equipment carried aboard took at last the veil off its invisible face.

The details of this feat are still sufficiently well remembered to require little repetition. A preliminary report on the photographic data obtained in the course of this flight and televised afterwards to Earth was released by the U.S.S.R. Academy of Sciences in December 1959 (*First Photographs of the Far Side of the Moon*, the English translation of which was published by the Pergamon Press, London, in 1960); while a definitive discussion of the entire material followed a year later in a volume the English edition of which is under review.

This volume summarizes the results of an exhaustive study of the topographic as well as photometric features of all available negatives, carried out independently at the Pulkovo Observatory, Sternberg State Astronomical Institute, Moscow, and the Kharkov Observatory, under the respective guidance of Profs. A. A. Mikhailov, Yu. N. Lipskiy and N. P. Barabashov—all well-known students of the Moon. The outcome of their impressive study (the methods of which are described in the first part of their book) resulted in the identification of 498 details on the lunar far side, the catalogue of which (classified according to their degree of reliability) constitutes the major part of the whole volume. The formations discovered on the far side of the Moon do not, in general, differ from those we know on the visible face in their photometric or topographic characteristics—though even a cursory glance at the first photographs of the far side revealed a much greater preponderance there of mountainous areas (and a corresponding scarcity of the maria) than is the case on the side that is familiar to us.

The last, and most valuable, part of the present volume consists of the reproductions of 30 frames of the individual photographs secured by the Russian space station. Needless to stress, no one frame reveals all the details ascertained for that particular region from the ensemble of the material; but the best single frames appear to attain a ground resolution of some 10 miles.

A map of the far side of the Moon, showing the distribution of topographic details listed in the catalogue, concludes the whole volume. It is the first map of its kind, and comparable in amount of detail with maps of the visible face of the Moon available by the first half of the eighteenth century.

All considered, the scientific outcome of the flight of the Russian third space station must be regarded as a splendid success, and a wonderful achievement in which the Russian nation and all their fellow inhabitants of this Earth can justly rejoice. It does not mean that the days of discovery on the Moon are completely over; for a small part of its surface (approximately 40° in longitude) was not visible from the Russian space station at the time of photography and remains, therefore, still uncharted. It will, however, certainly not be long before even this remaining *terra incognita* of the Earth–Moon system will reveal its secrets to the inquisitive eye of the next lunar circumnavigating device, and the pioneer days of lunar mapping will irretrievably belong to the past.

The volume under review constitutes without doubt an important landmark in selenographic literature, and Pergamon Press is to be commended for the speed with which it introduced it to the English reader. This speed entailed, however, also some obvious drawbacks; for by its external appearance the English edition (printed in Poland) does not come up to the quality of the Russian original; and the translation is decidedly weak—in marked contrast with the professional fluency and manner in which the preliminary report was translated, the year before, by Sykes.

Zdeněk Kopal

IONOSPHERIC RESEARCH DURING THE INTERNATIONAL GEOPHYSICAL YEAR

Some Ionospheric Results obtained during the International Geophysical Year

Proceedings of a Symposium organized by the U.R.S.I./A.G.I. Committee, at Brussels, Belgium, September, 1959. Edited by W. J. G. Beynon. (U.R.S.I. Monographs.) Pp. xi+401. (Amsterdam : Elsevier Publishing Company ; London : D. Van Nostrand Company, Ltd., 1960.) 72*s*.

DURING the International Geophysical Year a vast mass of data was accumulated by investigators of the ionosphere all over the world and some considerable time must elapse before these data have been analysed and fully interpreted. The purpose of the symposium with which the present volume deals was to discuss the preliminary results derived from the data.

The book contains sixty papers contributed by many of the leading ionospheric workers. All papers are written in English and some of them have summaries in French. They are grouped in approximately equal numbers under the headings : (1) *F*-2 layer phenomena, (2) high-latitude studies, (3) disturbance phenomena, (4) ionospheric irregularities, (5) $N(h)$ profiles, (6) absorption, (7) drifts, and (8) noise, whistlers, rockets and satellites. The first section contains papers on such topics as the equatorial anomaly in the *F*2-layer, the world distribution of ionization in this layer, and on the forecasting of world values of ionization density. Section (2) is mainly concerned with the morphology of sporadic-*E* ionization and of black-out in polar regions. In section (3) there are eight papers, most of them very brief, on ionospheric storm phenomena. Two other papers in this section deal with the effects of the two Johnston Island nuclear explosions in the ionosphere and on radio signals traversing it. The phenomena of spread-*F* and sporadic-*E* ionization are considered in section (4) where some interesting observations of both phenomena in equatorial regions are described. Some of the early results of calculation of the variation of ionospheric electron density with height above Earth are given in section (5). Of particular interest in this section are contour charts, for four separate times of day, showing the variation with height of the plasma frequency along the 75° W. meridian.

Section (6) deals with investigations of ionospheric absorption by the pulse reflexion method and by measurement of cosmic noise. Section (7) is noteworthy for three Russian papers on movements of ionospheric irregularities and for a preliminary report on the results of world-wide measurements of horizontal drifts in the *F*-layer. The papers on atmospheric noise in section (8) include a short summary of the measurements made throughout the world ; no results are given in this paper but the

section includes other papers giving results obtained in both the U.S.S.R. and Japan. Rockets and satellites are dealt with by American authors: one paper is a very concise record of the results of ionospheric measurements by American rockets; the other paper deals with the determination of total ionospheric electron content below a satellite by Faraday rotation observations.

As all these papers were written very soon after the end of the International Geophysical Year it is not surprising that many of them contain information of a very tentative character, and others are little more than brief reports on phenomena in a very early state of investigation. Indeed, some of the papers have been made obsolete by later publication by the same author before the appearance of the present volume. It is, nevertheless, a useful record of the symposium and is well edited and well produced. It is a pity that its high price will deter many workers from adding it to their private bookshelves.

A. F. WILKINS

PRANDTL'S COLLECTED PAPERS

Ludwig Prandtl

Gesammelte Abhandlungen zur Angewandten Mechanik, Hydro- und Aerodynamik. Herausgegeben von Walter Tollmien, Hermann Schlichting und Henry Görtler, Schriftlietung F. W. Riegels. Erster Teil: Pp. xix + 1–574. Zweiter Teil: Pp. xiii + 575–1071. Dritter Teil: Pp. xiv + 1071–1620. (Berlin: Springer-Verlag, 1961.) 273 D.M.; Ganzleinen 288 D.M.

THE monumental work of leaders of nineteenth-century physical science, such as Helmholtz, Kirchhoff, Kelvin, Maxwell, Boltzmann and Rayleigh, in creating a structure of concepts by means of which physical and engineering phenomena could be understood and predicted, was of such comprehensive character that the task of those who had to follow them and lead the way to the explanation of the mysteries that remained was formidable indeed. No hope lay in continued logical building on the structure of their predecessors. On the contrary, completely new intuitions were required.

The scientific public knows well how these were introduced into the physics of atoms, molecules and radiation by Planck, Einstein, Rutherford, Bohr and the rest. The revolution in mechanics is less well known. No better grasp of it can be attained than by a study of these three admirably produced volumes containing the collected papers of the leader in that revolution, Ludwig Prandtl.

The mystery in this field at the turn of the century was thickest in the mechanics of liquids and gases. Three of the eight main groups of papers into which these volumes divide Prandtl's work are devoted to the three outstanding new intuitions by means of which light was to be shed on that mysterious subject.

The first of these, chronologically speaking, a joint achievement of Stodola and Prandtl, was the elucidation of steady supersonic flow, stimulated at the time by the requirements of steam turbine nozzles, though later to become the foundation of supersonic aerodynamics. It included a full description of the effect of varying the nozzle back-pressure, through and beyond those values which force supersonic flow to terminate at a normal shock-wave in a range of positions and strengths, to the values where a supersonic jet is produced, the structure of which was sketched by means of the ideas of oblique shock-waves and of what were later to be called Prandtl–Meyer expansions. A preliminary theory of shock-wave structure was also obtained in these early years. Prandtl's later work on gas dynamics, with Busemann, evolved a highly versatile and accurate theory of two-dimensional supersonic flows, using the geometry of their characteristics, and so derived jet shapes and flows about aerofoils with closer experimental agreement. It is interesting to note too, in this group of papers, not only the detailed studies of the effect of compressibility in subsonic flow but also a short work of 1938 giving clear warning of supersonic bangs and considerable detail about their geometry.

The famous elucidation of the true role of viscosity followed closely that of compressibility, the paper stating all the essential properties of laminar boundary layers being presented in 1904. The nature of turbulent boundary layers was appreciated soon afterwards, and a 1914 paper used the two concepts to explain the extraordinary vagaries in the drag of spheres. Each of these well-known papers includes a lovely *experimentum crucis*. Later investigations in the group of papers devoted to boundary layers and frictional drag relate to the law of turbulent resistance of smooth and rough pipes and plates.

The third new branch of fluid dynamics created by Prandtl, perhaps the one of greatest technological importance, was the theory of lift and lift-induced drag. It was a complete lifting surface theory that Prandtl, with his pupils Betz and Munk, derived and applied to monoplanes, biplanes, propellers and other systems. As might be expected, the largest section of Prandtl's collected papers is devoted to all its ramifications.

The volumes are a reminder, nevertheless, of the outstanding achievements of Prandtl in fields quite different from those so far mentioned. A long section devoted to elasticity, plasticity and rheology reminds us of Prandtl's striking contributions (followed up by his pupil von Kármán) to a reconciliation of theory and experiment in elastic stability. We recognize, too, his early appreciation of the practical significance of 'perfect plasticity' theory, which he elaborated mathematically on lines parallel to those of the supersonic flow theory to illuminate hardness tests, extrusion and the like, and which, with his work on permanent set, rupture, and materials the stress-strain relations of which include a relaxation time, helped to create the mechanics of solids as we know it to-day.

Another section is devoted to vortex development and turbulence, including the rolling-up of vortex sheets, flows past sharp edges, rotating cylinders, etc. In turbulence theory proper, Prandtl's momentum transfer theory attached too little significance to the role of big eddies, but the theory and associated experiments illuminated to a substantial degree the effect of temperature gradients on turbulence and, conversely, of turbulence on heat transfer, as well as a host of complex phenomena such as the secondary flow in straight pipes of non-circular section.

The meteorological section includes Prandtl's computation of the distribution of wind velocity and direction near the ground (Ekman spiral) using a turbulent exchange coefficient. It includes also his contribution to the understanding of why the west–east momentum in the general circulation of the atmosphere is transported on the average at a positive rate from the tropics to the temperate zones (even

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though any 'random' mechanism would cause it to flow the other way, down its gradient). Prandtl noted, in this context, that any loss of energy in the high-altitude west–east circulation (due to large-scale disturbances) would reduce the Coriolis force balancing the poleward pressure gradient, and so permit poleward movement down that pressure gradient until the energy had been restored; and he noted also that the geostrophic relation between poleward pressure gradient and west–east momentum implies that energy-restoring motions must also make the west–east momentum flow polewards. Other illuminations in this field include work on the structure of fronts, and, remarkably enough, an original paper dated 1950 on the dynamics of the jet stream.

The volumes close with a section covering many of Prandtl's significant contributions to experimental technique, which laid the foundations of modern low-speed and high-speed wind-tunnel practice (and, as a curiosity, included experimental studies in a rotating room), followed by a group of miscellaneous papers, among which stand out a beautiful piece of work on bearing lubrication and some eloquent advocacy of the use of vector analysis.

Those who love theoretical and applied mechanics can be recommended, if necessary, to curtail some future holiday in order to be able to afford these absorbingly interesting volumes. Such a drastic measure might also enable them peacefully to enjoy the pleasures of their first perusal!

M. James Lighthill

THEORY OF BOUNDARY LAYERS

Boundary Layer Theory

By Dr. Hermann Schlichting. Fourth edition. Translated by Dr. J. Kestin. (McGraw-Hill Series in Mechanical Engineering.) Pp. xx+647. (New York: McGraw-Hill Book Company, Inc.; London: McGraw-Hill Publishing Company, Ltd., 1960.) 128*s*.

New Methods in Laminar Boundary-Layer Theory

By Dr. D. Meksyn. Pp. xxiv+294. (London and New York: Pergamon Press, 1961.) 70*s*. net.

THE concept of the boundary layer was discovered by Prandtl in the first years of the present century, and since then it has occupied a central position in fluid mechanics. The boundary layer is essentially a skin effect, which occurs in the flow of a fluid with small viscosity, but the behaviour of the layer may have a profound influence on the general character of the whole flow. For this reason, the mechanics of the boundary layer is of great importance to engineers and mathematicians interested in the problems of fluid flow. In recent years the study of boundary-layer flow has attracted increasing attention, both theoretically and experimentally, and a great number of papers have appeared on this subject.

Prof. Schlichting has been one of the leading contributors in this field, and his book, which was originally published in German ten years ago, has now appeared in its fourth English edition. This follows the same general plan as the first German edition, but the accretion of new material has made it considerably bigger. The first part provides the basic physical ideas and the fundamental equations for the flow of viscous fluids. Some of the exact solutions of these equations are discussed, and there is a chapter on the approximate solutions which are valid when the viscous forces are dominant over the inertia of the fluid. Laminar boundary layers are treated in the second, and longest, part of the book. This side of the subject is the most fully understood, and has received extensive mathematical treatment. A full account of two-dimensional flow is given, including chapters on heat transfer and compressibility. Axisymmetric and three-dimensional boundary layers are treated more briefly, and there is a chapter on boundary layer control.

The third part is on the transition from laminar to turbulent flow. It contains a description of the theory of hydrodynamic stability, its experimental verification and its relation to the formation of turbulence. The factors influencing stability are considered, with applications to the flow over aerofoils. The last section of the book deals with fully developed turbulent flow. Here the treatment is of necessity largely empirical, and based on the analysis of experimental results. Separate chapters deal with flow in pipes, over flat plates, with the calculation of turbulent boundary layers, and with free turbulence in jets and wakes.

Schlichting's book is written for engineers, and emphasis is placed on those methods and results which are likely to prove most useful. Topics which are not yet amenable to routine calculation, such as the flow over a general three-dimensional surface, are dealt with only briefly. Each chapter has an extensive list of references, and there are many figures illustrating theoretical results and experimental observations. In a book on such a quickly growing subject there is inevitably scope for improvement and addition in detail, but it is likely to remain a standard work for several years. The legend of Fig. 5.15, on page 90, has an error, and a corresponding one is made in the description, on page 91, of the effect of Reynolds number on the flow in a divergent channel. The book is well produced and clearly printed.

The scope of Dr. Meksyn's book is more limited, as its title indicates. It is concerned with mathematical methods, and deals mainly with steady laminar flow and with stability theory. The author has written several papers on these subjects since the War, and his book presents a systematic account of his work. Other aspects of laminar boundary layers are mentioned rather cursorily. The reader who is already familiar with boundary-layer theory may find Meksyn's methods of interest, but he would be well advised to check the formulæ carefully. The original papers contained several errors, of which most have been corrected, but some still survive. There are a number of minor slips.

E. J. Watson

MEASUREMENT OF WATER-FLOW

Hydrometry

Theory and Practice of Hydraulic Measurements. By Prof. Adam T. Troskolanski. Pp. xix+684. (London and New York: Pergamon Press; Warszawa: Panstwowe Wydawnictwa Techniczne, 1960.) 120*s*. net.

WHEREAS in most other countries 'hydrometry' means the science of water-flow measurement, in Britain it has been connected with measuring the density of liquids. The title of this book is therefore yet another example of a distinguished foreigner teaching us our own language.

Although water-flow measurement is one of the oldest sciences, it has not been well documented and we are therefore indebted to Prof. Troskolanski for providing a comprehensive survey of the subject. Before entering the Technical University of Wrocław, the author was chief engineer of the Polish National Bureau of Measures and therefore with authority, both as engineer and scientist. He has confined himself mainly to water-supply engineering, although water-flow measurements for the hydro-electric industry are mentioned briefly.

This new book is an enlarged version, in English, of Volume 3 of the author's text-books *Hydromechanika Techniczna* and includes new chapters on recent advances, such as magnetic flow-meters, radioisotope techniques and water-level measurements by γ-ray probes.

The three main sections are : (1) units, and principles of measuring length, area, volume, time, pressure, velocity, flow-rate and total flow ; (2) instruments and techniques for measuring these physical quantities ; (3) laboratories for calibrating instruments and absolute standards of flow measurement.

The subject is dealt with logically and in considerable detail. All equations are dimensionally consistent, but in addition both British and metric units are used throughout. The author's philosophy is that measurement of the flow is a special branch of metrology, depending fundamentally on measurements of length, time, etc. Such basic aspects are covered in detail in the first section, leading up to the measurement of flow-rates and total flow.

It is difficult to understand why the translator preferred "intensity of flow" to the more widely used term "flow-rate". Similarly, "potential-head" is used rather narrowly. It is not generally the same as the height of filling of a tank, unless the bottom of the tank is the zero potential datum. However, despite such minor criticisms, the translated text is lucid and much careful revision has gone into the notation, where even the mnemonic subscripts have been translated into English. British standards have been widely used and quoted.

The second section gives a full account of measuring instruments and recorders, including several not usually described in English text-books, such as the Andersson travelling screen, measuring cascades, Danaides, and the detailed analysis of current meter performance and calibration. Instruments used in water-supply practice, such as level gauges, constriction and mechanical flow-meters, are particularly well described.

The final section, on hydraulic laboratories and meter calibration, provides the sound foundation which is so often missing in books on measuring instruments. Accurate calibration is essential, and it is valuable to have detailed descriptions and recommendations for reliable test facilities.

The descriptive material is excellent and is well illustrated, together with many physical tables and a comprehensive index in English, French and German. Some of the information about fields other than water supply is a little out of date. For example, both the Allen and Gibson methods have now been accepted internationally for the latest International Electrotechnical Commission code for water turbine testing. Sodium chloride has been largely superseded by other chemicals in the salt titration technique.

The Allen salt-velocity method is reviewed more unfavourably than it deserves in view of its successful use in the United States and elsewhere. On comparative flow measurement tests no more recent references than the Walchensee tests of 1926 are quoted, nor is it made sufficiently clear that the weir is a secondary method of flow-measurement and for highest accuracy must always be calibrated.

However, in general this is a most valuable collection of detailed information, set out clearly and logically, on a subject which until now has not been well documented. It can be recommended to all hydraulic engineers interested in flow measurement.

S. P. Hutton

A HISTORY OF METALLOGRAPHY

A History of Metallography

The Development of Ideas on the Structure of Metals before 1890. By Prof. Cyril Stanley Smith. Pp. xxi+291. (Chicago: University of Chicago Press; London : Cambridge University Press, 1960.) 8.50 dollars; 68*s*.

THIS volume, which has been eagerly awaited by those aware of its preparation, was worth waiting for. In the author's own words, "Perhaps the study even has a certain timeliness, for it is abundantly clear that the proper balance between 'applied' and 'pure' science that is necessary for technological and cultural well-being has yet to be achieved".

Broadly the book is divided into three main sections, first the background of metallography in ancient works of art, then the philosophical background and the observations of structure before the use of the microscope, and finally, the period of increasingly active observation and theory from the time of Sorby onwards. It is a story that involves the history of art, of 'natural philosophy' and of technology, and ends about 1890, by which date metallography had begun to be recognized as a definite discipline in its own right, though Chapter 16 does carry the story down to recent years. Two appendixes give in full a paper of Sven Rinman of 1774 on "Experiments of Etching upon Iron and Steel", and Sorby's paper of 1885 to the Iron and Steel Institute "On the Microscopical Structure of Iron and Steel" which differs considerably from the version published in 1887 and of which few are probably aware. A long list of bibliographical notes bears testimony to the extent of the sea over which the author has cast his net, the catch being a work of real scholarship as well as a first-rate contribution to the history both of science in general and of metallurgical technology in particular.

The earlier portion of the book dealing with the relation between æsthetic appearance and structure is concerned with the fact that, long before it was appreciated by the philosopher that metals are aggregates of innumerable small crystals randomly packed together, this existence of 'structure' was used by the artisan to produce his effects. "Differential chemical attack was used in Europe to give a decorative mark of quality to swords as early as the second century A.D., but the technique passed out of use" though in the East surface texture did continue in use for this end. "The superiority of the swords of Damascus and Japan stemmed directly from the fact that the smith related a certain visible texture to the serviceability of the weapon and adjusted his manufacturing process to produce it." That metal workers have been on occasion intuitively sensitive to the

inner structure of their materials and have empirically developed ways of revealing it there can be no doubt, and such observations clearly led to the deliberate choice of manufacturing methods as well as of a kind of metallographic control over the working and heat-treatment processes required in order to obtain the surface structure desired both for beauty and service.

The section which describes the gradual development of the idea of a metal as an aggregate of crystals is the most substantial and, in many ways, the most interesting of the whole book. The anti-Aristotelian trend of the early seventeenth century paved the way for renewed consideration of the inner nature of metals, and Descartes himself must have been a close observer of the operations of the iron-smelters and of the smith. In 1639 he was in correspondence with Mersenne regarding the reason for the hardening of steel, and it is quite clear that he had watched the production of wrought-iron during its manufacture in the finery hearth: "The whole bath of molten metal becomes divided into many small lumps or drops, the surfaces of which become smooth". Although these early ideas were necessarily crude, often inaccurate, and, from a modern point of view, often bordering on the fantastic, Rohault, in 1671, in his *Traité de physique*, when discussing the properties of ductility and hardness, could say "we cannot but think that the component Parts of Metals are long; otherwise we cannot understand how Metals should be so ductile as they are, whether they be forged upon an Anvil or drawn through a wire-drawing Iron; whereas if we suppose them to be somewhat long, it is easy to conceive, that when they are pressed on one Side, they slip sideways of each other without quite separating. Further—we cannot but think that they must necessarily so order themselves as to place themselves by each other's Side, and correspond Length-ways to the Length of the whole Piece, which will make it easier to bend that Way than any other—And we find Strings in them, as in the Slip of an Ozier. These Strings ought not to be in a Metal that is cast and has not been forged: And so we find that cast Metal is as easy to break one Way as another". It was, however, left to de Réaumur to develop such corpuscular theories into something useful, and a century before the 'particles' of such theories had developed into the chemical atom on one hand, and the stacking of polyhedra had given rise to mathematical crystallography on the other, Réaumur was using the idea of 'parts' aggregated together on different scales to develop theories regarding the nature of iron and steel and to explain the structures which he saw on fractured metals.

The final section, essentially the work of Sorby and his successors, brings the story down to men known personally to the older generations still alive. Sorby himself, Arnold, Stead, Sauveur and evidently to the author Martens and Osmond in particular all play their parts. The bitter controversy which raged regarding the relative importance of carbon or a hard allotrope of iron is recalled, and it is perhaps not without a feeling of justice to those on both sides to remember that, to the best of our present-day knowledge, the true explanation contains an element of both theories. As McCance was probably the first to suggest explicitly, a highly distorted iron lattice, the distortion being due not to allotropy but to the high state of supersaturation of carbon in the quenched steel, is as near as the ordinary metallographer probably needs to go.

Beautifully produced and illustrated, this is a book which both Prof. Smith and the publishers will look on with real pride.

F. C. Thompson

THE MECHANICS OF VIBRATION

The Mechanics of Vibration

By Prof. R. E. D. Bishop and Prof. D. C. Johnson. Pp. xii + 592. (Cambridge: At the University Press, 1960.) 120s. net.

THIS is a book written with painstaking care on the subject of the basic principles of mechanical vibration and their application to the study of specific problems. Its title and contents direct attention to the diversity of meanings that may be attached to the word "mechanics". To some engineers this book, being largely algebraic, will appear to be abstrusely mathematical; to a mathematician the mathematical operations in it are elementary. The engineer may be appalled by the authors' insistence (on p. 96) that they are restricting their attention to the mechanics of vibration and that the mathematics is a separate subject that they hope to present in another volume. He may clutch at a straw floating on p. 114 because it suggests that the mathematical part of at least one problem may be "reduced to arithmetic". The quantity of arithmetic involved in some solutions, however, implies a generous interpretation of the word 'reduced'.

A good deal of space is rightly used in demonstrating applications of the concept called 'receptance' in 1954 after earlier use of the name 'mechanical admittance' for it by Prof. W. J. Duncan in *Reports and Memoranda* No. 2000 (1947) of the Aeronautical Research Committee, mentioned in several places in this book. It may be added that the application of this concept to mechanical problems is much older than either of these names for it.

A chapter on "The Analysis of Real Systems" begins with a quotation from Routh and refers to Rayleigh's principle, Dunkerley's method and Southwell's theorem in a succession that directs attention to nice distinctions in nouns.

It is remarkable to find, in this book, a suggestion that for the purpose of calculating its natural frequencies, a system of rotors and shafts in series may be replaced by one composed of distributed masses, merely to avoid the Holzer tabulation which is laborious for a system of more than 3 or 4 masses. The Holzer procedure is in fact a good way of calculating relative amplitudes of vibration for a known natural frequency, but as a means of determining frequencies it is at least thirty years out of date and ought never to be used for that purpose either with or without electronic 'brains'. The rational procedure is a routine well within slide-rule range.

In Chapter 7, reference is made to the method of estimating the lowest natural frequency of flexural vibration of a small non-uniform beam and the calculated value is compared with that determined by actual trial. The smallness of the discrepancy inspires confidence in the mathematical procedure but without weakening the impression that where instruments for exciting and measuring vibration are available, testing of a model is a quicker and more reliable alternative to calculation as a means of determining natural frequencies of certain types of systems.

The chapters on damping of vibration show that even when the usual drastic assumptions are made about the quantitative characteristics of damping, it is a seriously complicating circumstance in analysing any but the simplest vibrating systems. Abandonment of those assumptions leaves difficulties that cause the authors to remark that "The assessment of damping is a subject in which research is needed". This describes with great delicacy the present state of knowledge of this particular subject.

In the last chapter the authors introduce the subjects of "Non-harmonic Vibration and Transient Vibration" and show them to present much more formidable analytical problems than any solved by the authors or others in the subject of harmonic vibration. Reflexion on this helps one to understand why some practical problems in vibration are analytically refractory and perhaps analytically insoluble.

Any mechanical science graduate who studies this book and works through its numerous and excellent examples ensures for himself a thorough grounding in the theory of mechanical vibrations.

W. A. TUPLIN

INDUCTANCE COILS

The Theory and Design of Inductance Coils

By Dr. V. G. Welsby. Second edition. Pp. 232. (London: Macdonald and Co. (Publishers), Ltd., 1960.) 30*s*. net.

DR. WELSBY'S book on the design of inductance coils, first published in 1950, has now reappeared as a revised second edition. Those who are familiar with the first edition will know that the book contains very extensive formulæ for the calculation not only of the inductance of coils but also of the effective resistance and the effective shunt capacitance. The coils considered are air cored with solid and stranded wire, and those with laminated ferro-magnetic cores, with dust cores, and with ferrite cores. The theoretical treatment given is not always as detailed as in the original papers but references are given for those who wish to study the theory fully, while the theory and formulæ given in the book are fully adequate for all whose main concern is to design and make efficient coils.

The author is careful to explain the limitations of theoretical formulæ for coils with magnetic cores, but a slight amplification of the parts of the book covering experimental results and methods of correlating theoretical formulæ with these results would add to the practical value of the book.

The two principal changes in the present edition are the use of M.K.S. units and the use of the principles of electromagnetic wave propagation to derive some of the formulæ. Both changes represent an improvement, but in both cases the new material is not entirely happily welded into the old. It is difficult to justify the author's use of the symbol η in place of μ_0 for the magnetic constant of space, the use of μ in place of μ_r for relative permeability, and the use of μ_0 for initial permeability, except on the basis of preserving inviolate some of the formulæ given in the first edition. The factor 10^{-9} is also to be seen in many of the formulæ instead of the factor 10^{-7} more usually associated with M.K.S. formulæ.

The theoretical treatment tends to be most detailed for the simpler parts and to be uncomfortably condensed for the difficult parts. In particular, clearer and more detailed explanations of the method of applying field theory to the solution of coil problems would be advantageous. It is rather surprising also, in view of the author's liking for field theory, that capacitance is treated as if it were in shunt across the coil terminals and not as a distributed effect.

These minor defects should not be allowed to obscure the real value of the book, covering in the space of 230 small pages a great quantity of most useful information not readily found elsewhere.

A. H. M. ARNOLD

DIFFUSION AND HEAT FLOW IN LIQUIDS

Diffusion and Heat Flow in Liquids

By H. J. V. Tyrrell. Pp. xii + 329. (London: Butterworth and Co. (Publishers), Ltd., 1961.) 65*s*.

THOUGH somewhat uneven in its treatment of various themes, this book is a valuable and scholarly addition to texts dealing with certain irreversible phenomena in liquids. Chapters on the principles of non-equilibrium thermodynamics, on concentration diffusion, and on thermal diffusion are informative and well balanced. Descriptions of experimental methods for investigating various kinds of diffusion processes cover present practice in a very useful way; by comparison, a chapter on thermal conductivity measurements seems much less extensive. Interpretation of the phenomena observed is presented in the form of discussions. This part of the book will probably need revision soonest, since experimental information in the fields examined is growing rapidly.

One chief difficulty in discussing the interpretation of transport processes in liquids stems from their correlation with viscosity. At present, there seems to be no widely applicable treatment for linking viscosity with diffusion, despite the great convenience of viscosity coefficients for describing certain types of relaxation in liquids. For liquids of very simple structure, viscosity coefficients for relaxation of simple macroscopic shear have been related theoretically with mass migration, for example in the theories of Eyring. However, Eyring's models do not deal with the variety of specialized micro-relaxation processes which can occur in liquids containing polyatomic molecules, and in ionic solutions and melts. Viscosity coefficients tend to be injected quite generally into interpretations of transport processes without adequate recognition or description of their limitations. This book does not avoid the difficulty. The author's discussion of liquid viscosities is very incomplete. This unavoidably restricts the assessment of various molecular models devised to represent transport processes in liquids, in terms of their structure.

Despite this gap in the discussion of transport processes in liquids, the present book can be commended to research workers and libraries, particularly those concerned with diffusion phenomena. Scientific interest in diffusion is widening. The author's discussions of work on the separation of components by thermal diffusion should help to promote technical advances in this field.

A. R. UBBELOHDE

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RADIOACTIVE WASTE DISPOSAL

Atomic Energy Waste

Its Nature, Use and Disposal. Edited by E. Glueckauf. Pp. xi+420+4 plates. (New York: Interscience Publishers, Inc.; London: Butterworth and Co. (Publishers), Ltd., 1961.) 95*s*.

THE days are long past when industrial wastes could be discharged uncontrolled to the environment, and the new atomic energy industry has developed in a period which has seen new legislation introduced generally for the control of environmental pollution and specifically for radioactive discharges. Strict legislation (described in one of the articles in the book), a very sensitive public awareness and an exceptional concern with health hazards within the industry have stimulated a considerable amount of research on radioactive wastes.

A considerable part of the research is reviewed in this book. It is concerned primarily with the fission products separated as waste in the processing of nuclear fuels, which are regarded as the source of ionizing radiations to be used for man's benefit. It develops in more detail, and indeed in considerable detail, some of the views presented by the editor in a paper to the Second International Conference on the Peaceful Uses of Atomic Energy, wherein the fission products were seen as a source of radiations, of rare and precious elements and of specific radionuclides available for peaceful uses of atomic energy.

The book concentrates on the utilization of the liquid fission product waste as a source of ionizing radiations. It is not a general text on radioactive waste disposal. The small-scale use of radionuclides and the wastes arising are deliberately excluded; there is no account of the wastes arising at nuclear power stations; and although one good chapter is devoted to dispersion of activity from chimney stacks, there is no account of the treatment of solid and gaseous radioactive wastes.

The book consists of seventeen separate articles. The first, nearly a quarter of the book, describes the fission process and the fission products, nearly half of it in tabular and graphical form. This article and one on radiation chemistry, though good in themselves, go into far more detail than is required for the discussion of radioactive waste disposal. By contrast, the articles on α-emitters in reactor wastes, effects of radiation on living cells, movement of radioactive substances in food chains and radiation protection present the broad aspects and concentrate on the essentials.

While the first half of the book, the introductory or background part, is somewhat uneven in its treatment of the topics covered, the second half contains good review articles of the processes and operations used in the treatment of liquid radioactive wastes, the design of irradiation units using packaged sources and the uses of ionizing radiations for agricultural research, food preservation and induction of chemical reactions.

The treatment, perhaps naturally, leans towards British practices. Space might have been found for a more detailed discussion of wastes from fuel processing in other countries and of wastes from the processing of fuel elements made from stainless steels and zirconium alloys. The work carried out in the United States on disposal in salt formations and by deep-well injection might also have been described. The therapeutic use of ionizing radiations is a less easily understood omission. Some comparison of radiations from nuclides and radiations from machines, particularly in food preservation, would have been valuable.

Only a few errors were noted. The last entry on p. 251, referring to the allowed discharge from the Atomic Energy Research Establishment, Harwell, should be 20, not "2". On p. 227, what is referred to as slow sand-filtration, a method of treatment of drinking water, is really the trickling filter process for sewage purification. In the glossary, the 'rad', a unit of absorbed dose, is defined as a unit of amount of radiation.

The book is authoritatively and well written and well produced. It should, as the editor intends, illuminate "the background from which future developments can emerge".

A. W. Kenny

AN AMERICAN TAPESTRY OF STATISTICS

Contributions to Probability and Statistics

Essays in Honor of Harold Hotelling. Edited by Ingram Olkin, S. G. Ghurye, Wassily Hoeffding, William G. Madow and Henry B. Mann. (Stanford Studies in Mathematics and Statistics, No. 2.) Pp. x+517. (Stanford, Calif.: Stanford University Press; London: Oxford University Press, 1960.) 52*s*. net.

THE name of Prof. Harold Hotelling is chiefly familiar to English students of statistics as one of the founding fathers of that branch of their subject known as multivariate analysis. His share in the foundations was laid in half a dozen outstanding papers of the early 1930's, and the bibliography given here shows that this period saw his major contribution to theoretical statistics and that later he has been more concerned with applications, chiefly to economics. It might seem strange, on the face of it, therefore, to find a volume of 38 papers offered to him on his sixty-fifth birthday by statisticians for the most part very much of the mathematical variety. But Prof. Jerzy Neyman's introductory article shows clearly that Hotelling has been a powerful formative influence in American statistics and provided it with much of the dynamic which got it really under way. Not only did his papers help, at a crucial time, to demonstrate to the American mathematical and statistical worlds that statistics could be, simultaneously, both scientifically useful and mathematically rigorous but, over and above this, he seems also to have had a talent, akin to genius, for picking students and staff of outstanding ability and firing their enthusiasm for statistics. The list of thirty such men (some no longer living) which Neyman gives is extremely impressive and of these about a score contribute to the *Festschrift*.

The papers included are all on topical problems of theoretical statistics; and it is not untoward that only a minority refer to Hotelling's own work, since, as has been said, his major theoretical contributions are now embodied in the corpus of statistical classics. There is no unifying theme here. The topic treated by any given author could have been predicted from his own previous publications with some accuracy. The only obvious difference between this collection and, say, the last volume of the *J. Roy. Stat. Soc.* (B) is that the papers here are slightly shorter on average. This reflects the fact that though the papers here tend to be more fluent and essay-like than a

typical journal article, they are, by and large, slighter. As a consequence, they are for the most part easy to read. But it would be a hopeless task to attempt to review all of them, or even to try to pick out objectively the most important. All I can do is to mention some that caught my fancy. These include the two offerings from England, by M. G. Kendall and M. S. Bartlett, the latter discussing his concept of quasi-stationarity which promises to be, in one form or another, a key idea in the future development of stochastic process theory. Bradley and Prendergast extend modern ranking theory which already owes much to the former author. Block and Marshak have an intriguing paper on a cognate topic. Roy and Bhapkar expound and develop the Pearson–Roy logical analysis of multiway contingency tables. But perhaps the tributes which do Prof. Hotelling most honour are the papers by Bowker and Wilks developing classical multivariate analysis, and that of Stein, who looks at it from the most recent Californian point of view.

D. E. BARTON

ANALYSIS ON RIEMANN SURFACES

Riemann Surfaces

By Prof. Lars V. Ahlfors and Prof. Leo Sario. (Princeton Mathematical Series, Vol. 26.) Pp. x + 382. (Princeton, N.J.: Princeton University Press; London: Oxford University Press, 1960.) 80*s*. net.

THE modern era of Riemann surfaces was ushered in by H. Weyl's book *Die Idee der Riemannschen Fläche*. Here we find for the first time the systematic development of the idea of an abstract Riemann surface as an analytic manifold of one complex dimension, essentially a space with local parameters related in such a way that two distinct parameters are regular functions of each other in their common region of definition. Since the Second World War there has been a tremendous development in the field and books have appeared by Nevanlinna, Pfluger, Schiffer and Spencer, and Springer, for example.

Ahlfors and Sario's *Riemann Surfaces* goes further than its predecessors. The first chapter contains all the necessary topology which plays a fundamental part in the theory. The next chapter introduces Riemann surfaces and some of the basic methods for treating them, subharmonic functions, and the problem and integral of Dirichlet, Rado's theorem about the separability of Riemann surfaces which follows in a particularly simple and elegant way, and the fact that a smooth Riemannian metric on a surface induces an essentially unique conformal structure, a result which is frequently stated but seldom proved. The third chapter treats functions with singularities on a surface by Sario's elegant method of normal operators and deduces the principal mapping theorems for planar surfaces, that is, those topologically equivalent to plane domains. Such surfaces can be mapped on a plane domain bounded by various kinds of slits. In the simply connected case, we obtain the closed or open plane or the unit disk.

The second half of the book consisting of the last two chapters is more for experts. The fourth chapter introduces a complete exposé of the modern theory of degenerate surfaces, that is, those not admitting functions of various kinds and their inter-relations. This subject was opened by Ahlfors in the late 'forties and the solutions of the problems raised by him have now been almost completely obtained by the authors of the present book and others. The last chapter treats differentials on arbitrary Riemann surfaces and finishes with a welcome section on the classical theory of integrals on closed surfaces and the Riemann–Roch theorem.

This is an authoritative and long-awaited treatise by two of the greatest experts in the field. The elegant formulation of many of the ideas and proofs have made it possible to include more material than there is in any other book on the subject. The presentation is fairly clear but the subject is difficult, and particularly in the latter chapters the approach is very abstract. If one wishes to have complete generality and at the same time prove the classical theorems, it is most economical in time and space to deduce the latter from the former; but it is not necessarily the easiest way for the reader. Although this book is completely self-contained, I should recommend it rather to those readers who already know something of the subject—having looked, for example, at G. Springer's *Introduction to Riemann Surfaces*—than to the complete tyro. As a reference book, however, and a complete survey of all techniques right up to the frontiers of the subject, it is unequalled, and every serious mathematical library should contain it.

W. K. HAYMAN

MODERN GEOMETRY

Lectures on Modern Geometry

By Beniamino Segre. (Consiglio Nazionale delle Ricerche—Monografie Matematiche, 7.) Pp. xv + 479. (Roma: Edizioni Cremonese, 1961.) 7,000 lire.

MODERN geometry is a term which has seen service in many campaigns and under many commanders. However, in the present instance, the use of the title is not only justified at the moment but also stands a good chance of remaining so for some time to come; for this book, which is a greatly enlarged version of an Italian original of 1948, completes in various respects a generalization which has been under way for centuries.

Algebraic geometry as we know it to-day stems from two main sources: the invention of co-ordinates, and the analysis of axiomatic structure. The latter process has given a whole series of shocks to intuition; these, once absorbed, have led to the creation of new geometries which find their natural expression in terms of suitable co-ordinate systems. In a definitive account this process may well be reversed; in Prof. Segre's work we have examples of both procedures.

Part I of the book is a lucid exposition of the algebraic concepts and results which are required later. A useful innovation here is the term corpus to denote a general field, the latter name being reserved for commutative corpora. Part 2 is devoted to the foundations of projective geometry over an arbitrary corpus. The first chapter deals with linear spaces, that is, geometry based on homogeneous point co-ordinates. In the second chapter, which is concerned with graphic spaces, the approach is axiomatic: a graphic space is any set of abstract elements ('points') which satisfy the incidence relations of projective geometry. On this basis one proceeds to erect a co-ordinate system.

At this point Desargues' theorem on triangles in perspective comes into play. It can be shown that the theorem holds in every linear space, but that there are graphic planes in which it is false. In contrast

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with the situation in higher space, Desargues' theorem in the plane is not a consequence of the axioms of projective geometry. A second group of results concerns Pappus' theorem (that is, Pascal's theorem for a line-pair): it may be proved that this theorem holds in a plane if and only if the corpus defining the co-ordinate system is commutative. Also the theorem cannot be established on the sole basis of the incidence postulates and Desargues' theorem; but Desargues' theorem can be deduced from these postulates together with Pappus' theorem.

There follows a very interesting chapter on finite linear spaces, a subject to which the author has made fundamental contributions during the past few years. It is here, in the geometry of a finite number of points, that intuition receives its gravest shocks and that seemingly unshakeable theorems tumble like ninepins.

A substantial appendix by L. Lombardo–Radice on non-Desarguesian finite graphic planes takes the theory further; but much has happened in the two years since the book went to press. The style and content of this work are such as we have come to expect of the distinguished author, whom all geometers will thank for this valuable addition to the literature.

L. Roth

"OPINIONS OF THE LATE AND BEST PHISITIANS"

Tobacco

Experimental and Clinical Studies—a Comprehensive Account of the World Literature. By Prof. P. S. Larson, Prof. H. B. Haag and Prof. H. Silvette. Pp. xii + 932. (Baltimore, Md.: The Williams and Wilkins Company; London: Baillière, Tindall and Cox, Ltd., 1961.) 160*s*.

In 1595, an anti-smoking tract appeared in England entitled "Opinions of the Late and Best Phisitians concerning Tobacco", establishing a tradition of criticism which has persisted to the present day. This reference does not appear in the book under review, but there can be few of scientific interest which are not included. The authors' stated intention is "to be deliberately non-selective, printing good work and bad, sound and uninformed opinion, alike, in the same type", for they discovered that "there was scarcely to be found consistency of data in any area of observation, and unanimity of interpretation was even more rare". The result is an enormous work with more than 6,000 references. It is not, however, an unevaluated mass of contrapuntal observations, echoing the disagreements of a century and a half, for the authors have decided views expressed by length of quotation, inclusion of critical reviews, and their own comments on methods and principles of research.

The authors are pharmacologists, and the first part is devoted to the pharmacology of tobacco in many species.

The human race has experimented on itself with tobacco so persistently that short-term effects due to nicotine must be relatively unimportant. It has been said that nicotine can be regarded as a naturally occurring hormone in regular smokers. It is not significant that it can be toxic in large doses; so, after all, is adrenaline. Since nicotine is the major constituent it has pride of place, and our ignorance of the other 150 constituents of tobacco smoke, 10 of which are carcinogenic, is startlingly apparent. In such chronic habits as smoking these 'tracer' substances must be as worthy of study as nicotine.

A large part of the volume is clinical. One feels that in referring to particular diseases the aid of specialist clinicians might have been an advantage. For example, the statement is made, correctly, that most authorities forbid smoking in thromboangiitis obliterans; but the patients observed by these authorities were almost certainly arteriosclerotic, and their conclusions will not stand up to critical appraisal.

This is a minor criticism. The authors' general critical approach could be imitated with benefit by many clinicians who are in the chase after chronic influences on chronic diseases.

In most cases one must agree with the authors that the correct verdict on tobacco is "Remanded for further evidence". The greater part of the literature is critical of tobacco, but in this instance quantity does not count. There is no disease from piles to coronary thrombosis for which it has not been blamed, but it has also been used to treat most of them. It would be a mistake to condemn it from puritanical tendencies, when there may be beneficial effects as difficult to demonstrate convincingly as its alleged disadvantages. One supposes that the habit is of some value to those who use it.

Kenneth Bloor

ÆTIOLOGY OF ALCOHOLISM: CONTROLLED OBSERVATIONS

Origins of Alcoholism

By William McCord and Joan McCord, with Jon Gudeman. (Stanford Studies in Sociology, 1.) Pp. xi + 193. (London: Tavistock Publications (1959), Ltd., 1960.) 35*s*. net.

This is an important work. It is a well-controlled study of a large group, of both 'normal' and 'pre-delinquent' boys, of which the original purpose was to consider the value in prophylaxis of criminality of guidance by trained social workers. A vast amount of information was obtained. In due course the boys grew up, and some of them became alcoholics. Thus for the first time we have unprejudiced information about the alcoholic, obtained before the onset of the disease. In other very numerous investigations the information necessary for evaluating pathogenesis has been elicited retrospectively and liable to many sorts of bias. In the work presented in this book, bias seems to have been eliminated—partly by the multiplicity of observers and observations; partly by the absence of any design, in the original scheme, of studying alcoholism; and partly by careful coding and rating techniques.

They find no support for some widely held views: for example, glandular diseases, malnutrition, oral tendencies, latent homosexuality, do not correlate with alcoholism. They list seventeen variables in the childhood background that did correlate with alcoholism. Six were highly important: (1) maternal alternation between affectionate and rejecting attitudes; (2) maternal deviance, for example, alcoholism, promiscuity; (3) paternal antagonism; (4) paternal escapism; (5) an 'outsider' in conflict with parental values; (6) absence of high demands on the child by the parents.

They believe that their results indicate that by such forces the alcoholic has had developed strong desires to be dependent, but these are incompatible with the self-image in the stereotype of the American male—independent, courageous, dependable and resolute. Drinking satisfies this by being a 'manly' pursuit, which yet satisfied dependency desires. (I found this less cogently argued than the rest of the book.)

They note differences between the personality of the pre-alcoholic and that of the developed alcoholic; and between factors that precede criminality in one, and alcoholism in another.

It would perhaps be dangerous to generalize from this investigation about the genesis of alcoholism generally—there are some apparent differences between the alcoholics that the McCords describe and those with whom I am familiar. Nevertheless it gives what appears to be valid and reliable information on an area in which hitherto we have had little but speculation. W. McAdam

THE BRITISH NATIONAL HEALTH SERVICE

The Genesis of the British National Health Service

By John Jewkes and Sylvia Jewkes. Pp. xi + 67. (Oxford: Basil Blackwell, 1961.) 6*s.* 6*d.* net.

THE human and financial implications of Britain's National Health Service are so tremendous that the significance of a survey by Prof. and Mrs. Jewkes cannot be overrated. They question the assumptions on which the National Health Service was established, challenge the validity of comparisons between Britain's centrally directed system and those of countries where the health services owe less to central direction and more to local enterprise, and have considerable reservations about whether or not the Health Service is as effective as its protagonists would proclaim.

In their essay, the authors make a critical examination of the belief that, before the War, the British medical system was seriously defective and that nothing short of a centrally controlled free system could provide appropriate remedies; further inquiries are to be made into the economic and social consequences of the National Health Service. As a basis for their inquiry, the Jewkes's have investigated the numbers and distribution patterns of doctors, dentists and nurses, the numbers of general practitioners in relation to the number of consultants, comparative mortality statistics and the way in which a health service might have developed if there had been no nationalized direction and control.

Their findings are disturbing. Although the statistics are not always revealing, it would appear that, even if the number of doctors has continued to increase under the National Health Service, the rate of increase has been no greater than that which obtained during 1921–39. The same can be said of nurses and dentists, and although, apart from our lesser number of dentists, British medical services compared favourably with those of the United States in 1939, the average American to-day is much better served; the gap between us continues to widen.

With the introduction of the National Health Service it was hoped that the distribution of doctors throughout Britain would become more even. Between 1911 and 1951 the geographical pattern remained largely unchanged and, although there was a slight gain in the number of doctors in more unpopular areas during 1951–59, the ratio still varies widely between north and south, spas and areas of heavy industry. Specialist services have improved under the National Health Service, treatment by medical consultants being now much more widely available. Nevertheless, the percentage of consultants to be found in the more attractive southern parts of the country has varied little between 1938 and 1957. Prof. and Mrs. Jewkes also indicate that the increase in the number of consultants owes much to the up-grading of men who, before the introduction of the National Health Service, were called general practitioners and whose titles alone have changed.

A frequent complaint before the Second World War was that too many doctors carried too many patients on their panels. Some improvements have taken place, but, since 1954, the position has deteriorated. Between 1952 and 1959, for example, the average number of patients per principal in under-doctored areas fell only from 2,851 to 2,745. The charge, too, that older people have received far less medical attention since the introduction of the Service is also refuted by the figures.

Two other points emerge from the survey. One is that, since the inception of the National Health Service, mortality-rates in England and Wales have not fallen more rapidly than in other Western countries. The second is concerned with the administrative pattern of medical services and suggests that "the more sweeping criticisms of the pre-war organization of British medical services are not to be trusted and that the view that the pre-war weaknesses could summarily be swept away by a centralized organization was over-sanguine".

The findings of this inquiry raise so many issues of national importance that many people will wish to see the promised surveys into the social and economic consequences of the National Health Service. Others will see that this inquiry is important not only for its own sake but also as an exercise in social science. In many parts of this essay, Prof. and Mrs. Jewkes take exception to statements made by Prof. R. M. Titmuss and others which were adduced to support the principle of a centrally organized health service. In so doing they themselves, however unintentionally, have raised the question of whether social scientists should begin with a view and look for information to support it, or whether more profitable discussion might ensue if the inductive method of physical science were applied more faithfully. Is this one of the reasons why so much of social science is still looking for its basic concepts? T. H. Hawkins

A NEW MEDICAL DICTIONARY

The British Medical Dictionary

Edited by Sir Arthur Salusbury MacNalty. Pp. xix + 1680. (London and New York: The Caxton Publishing Co., Ltd., 1961.) 210*s.*

THE appearance of this truly monumental work will be received with delight by everyone who has, systematically or occasionally, the need to consult medical journals. Coinage of new words and changed meanings for old ones have led to the emergence of an English medical vocabulary which has become almost the equivalent of a foreign

language to many old and new members of the profession. Now, following the devoted efforts of Sir Arthur MacNalty and a team of colleagues over more than a decade, here is the very book for which we have been waiting.

The production is of the highest quality, an important feature in a work which is bound to receive rough treatment. The binding is stout and arranged so that, when an entry is found, the pages do not curl back in that maddening way so typical of bigger books. (This one weighs 7½ lb.) The paper will stand up to thumbing and the layout and type make reading easy.

The quality of the 110,000 entries is in keeping with the standard of the appearance. Definitions are so clear and precise that room has been found to include many variations on a single theme. The term 'abscess', for example, is plainly described as a "collection of pus circumscribed in a cavity produced by tissue disintegration and displacement". The general entry, however, is followed by succinct explanations of more than 200 different kinds of abscess ranging from "atheromatous abscess", "bicameral abscess" and "collar-stud abscess" to "shirt-stud abscess" and "wandering abscess".

Each main entry is followed by its pronunciation, meaning and derivation, although readers are left to find out for themselves the pronunciation of secondary entries. Where there is doubt, the simplest form of spelling is used, 'hæmospermia', for example, being preferred to 'hæmatospermia' for the condition in which "blood is discharged in the semen". Where shortening might lead to confusion, each spelling is included. 'Hæmoblast', for example, is also listed as 'hæmatoblast' and 'hæmocytoblast', the actual definition appearing under the last-mentioned entry.

For those who like to know at least a little about men and women whose names have left their mark on medicine, the treatment of eponyms is satisfying. Baron von Munchhausen's connexion with his syndrome owes much to Richard Asher's historical knowledge and makes not only Munchhausen but also the entry 'come alive'. The note about Dimitri Ivanovich Mendeléeff and, then, his Periodic Law, makes light work of mendelevium, a new transuranic element announced by Seaborg in 1955. The latter, incidentally, shows how recently some of the words in this dictionary have been coined and how wide-ranging has been the search for them.

To complete this word-picture, words are included if they have any significance in medicine at all. Thus, 'circuminsular' and 'circumvolute' are defined with precision along with more obvious medical words like 'circumocular' and 'circumoral'. The only deliberate omissions are words which are obsolete or valueless; even here eponymous terms are included if they are still occasionally used in medical literature or have some historical interest. Finally, to ensure that nothing is omitted or causes obscurity, three useful appendixes provide a firm base with a list of anatomical nomenclature, a number of physico-chemical tables and specialized words used by pharmacists. The total result is a book of some 1,700 well-packed pages which will be kept up to date by cumulative annual supplements.

English-speaking readers who have close or remote connexion with medicine will wish to thank the publishers for their vision and courage in producing such a magnificent dictionary. They should see to it that all the editors of medical journals in countries in Europe and Asia who have been struggling to present articles in the English language should be informed of what could be a great aid to them. These, and all English-speaking readers, have cause to be grateful to the editor and his distinguished colleagues for labouring so long to produce such a distinguished work. Lexicographers, as Dr. Johnson knew, are held high in national esteem. With all his outstanding contributions to medicine, Sir Arthur MacNalty may have little thought that he is now most likely to be remembered as the editor of *The British Medical Dictionary*.

K. M. Hawkins

APPLICATIONS OF SCIENCE TO PEACEFUL USES

Current Trends in Scientific Research

Survey of the Main Trends of Enquiry in the Field of the Natural Sciences, the Dissemination of Scientific Knowledge and the Application of such Knowledge for Peaceful Ends. By Pierre Auger. Pp. 245. (New York: United Nations; Paris: Unesco; London: H.M.S.O., 1961.) 33s.

Prof. Auger's ambitious survey of the main trends of inquiry in the natural sciences and the dissemination and application for peaceful ends of such knowledge, and on the steps which the United Nations, its specialized Agencies and the International Atomic Energy Agency could take to encourage the concentration of such efforts on the most urgent problems having regard to the needs of the various countries was undertaken at the request of the General Assembly of the United Nations. This survey was carried out with the assistance of a special advisory committee and on the basis of texts prepared and supplied by the several agencies and other bodies. Nevertheless, the task remains formidable and indeed forbidding, for the selection or omission of particular features must remain a matter of personal judgment which is liable to challenge, and if it is not easy to discern the precise purpose which the survey will serve, Prof. Auger is to be congratulated on the courage and judgment with which he has discharged his mandate rather than criticized for particular omissions.

The survey is in three parts. The first, which occupies some 180 out of the total 229 pages, surveys the trends of scientific research, by functional divisions rather than academic disciplines, and is preceded by an excellent introduction on the development of research and the transition from discovery to application. Here, and also in some of the separate sections, as in those on mathematics, the physical sciences, the chemical sciences and the biological sciences, Prof. Auger attempts to set forth his conclusions as to the main trends in research, but in the applied sciences this is less frequently done and more open to criticism. In the second part of the report Prof. Auger reviews very briefly the main factors which affect the organization of scientific research and the dissemination of its results, while in the third are set forth the recommendations concerning the practical steps which might be taken by the United Nations and the Agencies to concentrate effort on the most urgent problems from a general point of view. By and large these two parts may well prove the most useful feature of the survey; the second part in particular should stimulate useful discussions, though here the absence of references is something of a drawback.

R. Brightman

SHORT REVIEWS

A Bibliography of the Honourable Robert Boyle, Fellow of the Royal Society

By Prof. John F. Fulton. Second edition. Pp. xxvi+217. (Oxford: Clarendon Press; London: Oxford University Press, 1961.) 50*s*. net.

THE late Prof. John Fulton's *Bibliography of the Honourable Robert Boyle* has now appeared in a second edition, almost thirty years after the first edition was published in the *Proceedings of the Oxford Bibliographical Society*. Addenda to the first edition were also published by this Society in 1933 and 1947. In its revised form this exhaustive bibliography, with its scholarly annotations, has now been issued in one volume by the Clarendon Press, Oxford. To this volume Prof. Fulton has contributed a new preface, in which attention has been directed to changes rendered necessary as the result of newly acquired information. The preface to the first edition has been reprinted with "some omissions, several corrections, and a few added notes". This preface also contains some interesting notes on the dispersal of Boyle's library. Major changes are few. The discovery by Miss M. E. Rowbottom (Wellcome Historical Medical Museum) in 1950 of a new and, incidentally, the earliest published writing of Boyle has necessitated an addition to the list of his works; and references to the large number of papers and monographs dealing with various aspects of Boyle's life and work that have appeared since the first edition have also been added. It is a great convenience to have all this information incorporated in a single volume; and historians of science, librarians, bibliographers, book collectors and antiquarian booksellers will all be permanently indebted to Prof. Fulton for his work.

V. A. EYLES

The Annual of the British School at Athens

No. 55, 1960. Pp. x+238+59 plates. (London: British School at Athens, 1961.) 63*s*. net.

THIS volume from the British School at Athens includes a variety of interesting material. It begins with a report on the rest of the pottery found at Karphi during 1937–39 with some observations on the relationship between the designs which appear on the painted wares and the patterns used for textiles. Then there is Part 1 of a survey of prehistoric Laconia from the Neolithic period into the Bronze Age and even, in some cases, continuing on to Hellenistic and Roman times. This is a little-known area, the scene of many incidents in the Homeric poems and other writings, and few excavations have taken place there. It is followed by a consideration of Minoan trade relations as reflected by the Minoan objects found in Cyprus. Four white 'lekythoi' in the National Museum at Athens are also described and some Euboean floral black-figured vases in the Museum at Chalcis. There is also a discussion of the shrine of Kodros, Neleus and Basile at Athens.

Work at Knossos is represented by reports on the excavation of a well containing Protogeometric and Geometric pottery and also of Protogeometric graves at Agios Ioannis. Several inscriptions at Chios provide the material for a review of the local early tribal organization, and a fragment in the Piraeus Museum forms the basis for a brief study of the cult of Apollo Delios. It is followed by interesting discussions of the Sibylline tradition at Delphi and of the connexion between the small clay nodules stamped with seal impressions, known as *cratulae*, and the Linear *A* accounting system. The volume ends with some further consideration of architectural questions concerned with the Temple of Poseidon at Sunium. Numismatics and later work are both represented in a survey of the influence of the base silver deniers made at Tours in the thirteenth century A.D. on the coinage of Frankish Greece. Altogether a useful volume full of good things.

JOAN LIVERSIDGE

Observations and Experiments in Natural History

By Alan Dale. Pp. viii+154+8 plates. (London: William Heinemann, Ltd., 1960.) 12*s*. 6*d*. net.

THE aim of this book is to appeal to young scientists. It is designed to encourage their own observations and experiments—two essentials for anyone taking up a scientific career.

The book consists of notes of observations and experiments carried out by the author and others, and also suggestions for the reader's own activities. Sometimes a problem is posed, and a line of experiment suggested, leaving the reader to discover the answer. Wherever appropriate, broad or detailed biological facts are included.

There are six chapters. The first is an introduction. The others cover: invertebrate animals, excluding insects; insects; vertebrate animals; lower plants; higher plants. As these titles suggest, a wide field is covered and, therefore, a little is learned about a lot. This prevents the book from being a specialist or text-book, and, instead, acts as a stimulus. This also accounts for the lack of continuity in style. Each chapter is written in note form, with titles and sub-titles. There are many small black-and-white figures, and eight black-and-white full-page plates.

The book should interest all young people with a natural curiosity, not only those with an eye on their future.

B. J. G. MAITLAND

Contributions to the Systematics of Oriental Termites

By M. L. Roonwal and P. K. Sen-Sarma. (Entomological Monographs. No. 1.) Pp. xiv+407. (New Delhi: Indian Council of Agricultural Research, 1960.) Rs. 12; 19*s*.

FIVE papers dealing with the systematics of termites from the oriental region are presented here in one volume, the publication and distribution of which would appear to have suffered a delay of more than three years. Related contributions by Dr. Roonwal and his colleagues have continued meanwhile to appear in a variety of scientific journals, resulting in some confusion in the chronological sequence of their series.

Four papers are short and deal with a variety of genera in several sub-families of the Termitidae. The fifth paper, comprising 181 pages and 46 plates, is a

revision of two genera of Kalotermitidae, *Kalotermes* and *Neotermes*, in which 29 species are re-described, measured in considerable detail and fully illustrated, and a further six species described as new. In addition a number of lectotypes have been designated, since it was formerly the more usual practice to give a series the status of co-types. It is noted that in some instances the lectotype selected is the only specimen at the authors' disposal, and would not appear to have been chosen from a series of co-types.

This revision of two important genera of oriental dry-wood termites is a valuable contribution to the literature of the Isoptera, reflecting credit on the authors and the Indian Council of Agricultural Research, which financed the work. It will be of much practical assistance to entomologists working in the region, and beyond, on the biology and control of these insects. W. V. Harris

Ornamental Trees for Garden and Roadside Planting

By S. A. Pearce. Chapters on Diseases by Derek A. Reid, and Insect Pests by Joyce van Konynenburg. Pp. 195+94 photographs. (London: W. H. and L. Collingridge, Ltd., 1961.) 35*s*. net.

THE author, who is on the staff of the Royal Botanic Gardens, Kew, in writing this book enjoyed the advantages of being able to refer to one of the finest collections of living trees.

He has succeeded in passing on to his readers his expert knowledge, for this well-produced book contains in its sixteen chapters most that nearly all those interested in trees for ornamental purposes should require to know when selecting the right tree to plant in the right place. Having made this selection, advice is given on the correct planting of a tree and its after-treatment, including an excellent chapter on dangerous trees and how to deal with these, with some useful information on a tree owner's liability.

Ninety-four good black-and-white illustrations and nine helpful line drawings are included. The student, however, who refers to the book may be a little disappointed in the absence of a good annotated diagram of a cross-section of a complete tree-trunk to illustrate the chapter on "Life of a Tree" and the omission of a paragraph on the *p*H of soils in the chapter entitled "Knowing your Soil". In keeping with the high standard reached by the author when dealing with the practical aspects of growing trees are the six chapters devoted to descriptive lists of these.

He is to be commended in arranging for the specialists Derek A. Reid and Joyce van Konynenburg to contribute the authoritative chapters on "Diseases" and "Insect Pests of Trees". F. P. Knight

Cork and the Cork Tree

By Dr. Giles B. Cooke. (International Series of Monographs on Pure and Applied Biology. Division: Botany, Vol. 4.) Pp. xii+121. (London and New York: Pergamon Press, 1961.) 50*s*. net.

CORK from the bark of the cork oak (*Quercus suber*) of southern Europe has been used by man from very early times and has been of importance commercially in Europe over a very long period. In spite of the advance of synthetic materials the demand for cork does not lessen, probably because natural cork has a combination of unique properties not to be found in other materials. A good idea of the manifold uses of cork in the modern world may be obtained from a perusal of this book. The author was previously director of research of a large crown cork and seal company in the United States and has obviously made a close study of cork and its many modern applications.

Last century, the cork oak was introduced to cultivation in many other parts of the world where the climate seemed suitable, often through the agency of Kew. No lasting success or commercial development resulted from this, however, and southern Europe and north Africa continue to meet the world demand for cork. Interesting details are given in the book of early planting of the cork oak in the southern United States and of a recent project to stimulate further planting there. There is also up-to-date and useful information on the cultivation and treatment of the cork oak in Portugal and on production and trade in cork in that country—the world's largest producer. The book contains chapters on the physical properties, chemical composition, and the manufacture of cork articles, and the many forms of composition cork so much used to-day. F. N. Howes

Studies in Paleobotany

By Prof. Henry N. Andrews, Jr. With a chapter on Palynology by Charles J. Felix. Pp. xii+487. (New York and London: John Wiley and Sons, Inc., 1961.) 94*s*.

THE appearance of a new and up-to-date book about fossil plants is of rare occurrence. In the event, a special welcome must be accorded to *Studies in Palaeobotany*, for Prof. Andrews writes with great clarity and his text is accompanied by numerous excellent illustrations, many of which are completely new or reproduced from publications not easily available to the majority of readers. The larger part of the volume is devoted to a systematic survey of the major groups of vascular plants, but there are separate sections dealing with more general aspects such as the evolution of the seed, Palæozoic and Mesozoic floras, fossil plants of the polar regions, and palæobotanical techniques. There is also a section on bryophytes, and Charles J. Felix has contributed a most useful chapter on the specialized topic of palynology.

Prof. Andrews argues in favour of a polyphyletic classification of the vascular plants, but many would not agree that all the evidence on which his arguments are based is sufficiently convincing. As one example, there may be noted the importance attached to *Aldanophyton*, the supposed lycopsid of Cambrian age. Very little is really known about this fossil, and there is no proof of its affinities, still less that it was a genuine vascular plant. It is true that the Lycopsida and Psilopsida were already co-existent during the Silurian, but there is no evidence as to which appeared first or whether they represent quite separate lines of evolution as polyphyletism demands. To me, it seems that the more conventional outlook, which regards the *Rhynia*-type as having provided the ancestral stock for the other groups of vascular plants, is still not seriously challenged.

Two errors need to be noted. Fig. 9–2*A* is not a reconstruction of *Calamophyton bicephalum* but of *C. primaevum*, and on p. 416 the Cathaysian flora is incorrectly stated to have overlapped the Angara province when, in actual fact, the reverse was the case. Alan Wesley

Introduction to a Submolecular Biology

By Albert Szent-Györgyi. Pp. xi+135. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1960.) 5 dollars.

FOR some twenty years Prof. Szent-Györgyi's interest has been in possible mechanisms by which the reactions in cells are co-ordinated in metabolism and in the transfer of energy. He has successively viewed this central problem from various physical points of view; first, the common-energy level or continuum theory, then the triplet state (in *Bioenergetics*), and now, in this new little book, the theory of charge-transfer complexes. Once again, the possible catalytic effect of water is emphasized, and the author's lucid and enthusiastic prose is reinforced by photographs of the colourful events which happen when various solutions of donors and acceptors are mixed and frozen. The results of extensive molecular orbital calculations by the Pullmanns are included, and serve as the backbone of the discussion, which considers the topics of drug action, adenosine triphosphate, the thymus gland and the living state. There are growing numbers of scientists interested in electron mechanisms in biology who will find this book most stimulating, and a source-book of problems for some years to come.

D. D. ELEY

The Falkland Islands

By M. B. R. Cawkell, Dr. D. H. Maling and E. M. Cawkell. Pp. xii+252+16 plates. (London: Macmillan and Co., Ltd.; New York: St. Martin's Press, Inc., 1960.) 18*s*. net.

THE relatively little-known Falkland Islands have had a most eventful history since human occupation reached them. Their initial discovery is still somewhat obscure, in spite of active research by the more politically minded writers of South America. In the present work, which is a worthy successor to that of the late Miss V. E. Boyson, the many facets of the islands are carefully described, although sometimes with less enthusiasm than others. This volume proceeds systematically from 'discovery', through the early and later developments to administration and the role of the church and the school. The more scientific aspects of the islands, the climate, vegetation, geology and structure, and bird life are admirably discussed and give the serious reader a very clear insight into the many problems of the islands. The selected bibliography which appears at the end of the book is of great assistance in following up any specific subject more closely. This volume should be read by those who are interested in the far-flung parts of the British Commonwealth, since it is clearly shown that the Falkland Islands is a well-developed colony.

R. J. ADIE

Water Supply

Economics, Technology, and Policy. By Jack Hurshleifer, James C. de Haven, and Jerome W. Milliman. Pp. xii+378. (Chicago: University of Chicago Press; London: Cambridge University Press, 1960.) 7.50 dollars; 60*s*.

THIS is an interesting but highly critical account of the problems of water supply in the United States approached through the eyes of two economists, Prof. J. Hurshleifer of the University of California and Prof. J. W. Milliman of Indiana University, aided by a physical chemist, J. C. de Haven. The work has been made possible through the Rand Corporation as part of a research programme.

The authors believe that many water supply professionals are living in an artificial world of their own creation without respect for economic principles and rationality. The present and approaching shortage of water and the proposed remedies are examined in the light of this belief. Many of the conclusions reached are as a result highly controversial. Much of the substance of the book will, however, be of considerable interest to those concerned with problems of the supply of water in other parts of the world. Questions of over- and under-investment, financial returns on outlay, pricing, water in relation to other economic commodities, local regional and national organization and control, technological advances, and the legal position so far as water is concerned are all critically considered.

A great deal of blame is laid by the authors on the imperfections in water law in the United States, where water rights are not clearly defined and cannot be transferred with ease as are rights in land and minerals, etc. As a result it is argued that the economic market processes that ordinarily direct resources to uses that maximize their productivity do not operate.

The establishment of clear property rights in water poses, of course, difficult problems. Water is sometimes a transient resource, sometimes in store, sometimes above and at other times below ground, sometimes even unwanted. But increasingly it is becoming a scarce resource in both semi-arid and humid areas, and capital will be increasingly invested to satisfy the public demand for more water. The plea of this book is that this capital should be wisely invested with due forethought and on sound economic principles.

W. G. V. BALCHIN

Population Redistribution and Economic Growth, United States, 1870–1950

By Simon Kuznets, Ann Ratner Miller, and Richard A. Easterlin. (Memoirs of the American Philosophical Society, Vol. 51.) Pp. xiv+289. (Philadelphia: American Philosophical Society, 1960.) 5 dollars.

THIS is the second volume of a three-volume project designed to link various indexes of economic growth to the redistribution of American population, under the direction of Prof. Dorothy Thomas and Prof. Simon Kuznets. In the first volume, which appeared four years ago, the difficulties of collecting and adjusting comparable time series of economic data for individual years since 1870 were described, and the validity of the estimates discussed. The present volume consists of three monographs, dealing respectively with the labour force in different States, with the regional growth of income and with the changing distribution and structure of economic activity.

In each of the three monographs there is noted a process of convergence of inequalities between individual States. Labour force participation-rates (that is, the proportion of the population in gainful employment), income per head, and structure of manufacturing all show this trend. The authors are content to describe what has happened, and do not attempt to theorize about the future, nor do they suggest that the process of convergence that they describe was a necessary condition of growth in the past 80 years.

XUM

The third volume will deal with the role of migration and the interrelations between economic and demographic variables. The whole project promises to be an important contribution to the study of American economic history and development. E. Grebenik

Advances in Enzymology and Related Subjects of Biochemistry

Vol. 22. Edited by F. F. Nord. Pp. v+567. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1960.) 105*s*.

THE twenty-second volume of this useful series contains three articles on metabolic topics, two about the mechanism of action of enzymes, one on practical techniques, two on more biological topics, and one on pure chemistry.

The sections of metabolism reviewed are the synthesis and hydrolysis of sulphate esters (by A. B. Roy), the biochemistry of sulphonium compounds, particularly with regard to transmethylation (by S. K. Shapiro and F. Schlenk), and the biosynthesis of cholesterol (by G. Popjak and J. W. Cornforth). The last-mentioned review follows appropriately the review on carotenoid synthesis in the previous volume.

An important article by D. E. Koshland on "The Active Site and Enzyme Action" summarizes the methods which may be used to label and identify the active centre of an enzyme, as well as putting forward some conclusions about the chemical mechanism of enzymatic catalysis. S. Shifrin and N. O. Kaplan discuss the binding of coenzymes by enzymes, principally in cases where this may be studied by spectroscopic methods.

The genetic control of enzyme activity, and the induced synthesis of enzymes, are considered in articles by J. R. S. Fincham and H. O. Halvorson respectively. These two articles emphasize the increasing interest in 'enzyme biology'.

Two articles are of great practical importance to the practising enzymologist. F. Turba gives a valuable account of the purification of enzymes by column chromatography, with many well-documented examples. J. Baddiley and N. A. Hughes give an up-to-date account of the chemical methods now available for the synthesis of nucleotide coenzymes and their analogues. E. C. Webb

Röntgenstrahlinterferenzen

Von Max von Laue. Unter mitarbeit von E. H. Wagner. Dritte, neubearbeitete und erweiterte auflage. Pp. x+476. (Frankfurt am Main: Akademische Verlagsgesellschaft, 1960.) 75 D.M.

IT is always interesting and instructive to read a book written by the founder of a subject and to see how he considers that it has developed since it began. Laue's book has, of course, been a standard work for many years and most other text-books have been based on it, either directly or indirectly. Modern treatment of diffraction theory, for example, is much nearer to Laue's treatment than to the more vital and productive, but less clearly rigorous, treatment through Bragg's law.

It is interesting, and not a little salutary, to see the difference between Laue's treatment of X-ray diffraction and that of British authors. He justifies this third edition by stating that a great deal of progress has recently been made in research on the structure of crystals ; yet this section of the book looks curiously old-fashioned, with its diagrams of diamond, graphite and fluorspar. The author's interests lie much more in diffraction by imperfect structures—liquid crystals, temperature-affected lattices and deformed crystals—than in the structures in which workers in Britain are mainly interested. The names that appear frequently in our text-books—Bernal, Lonsdale, Hodgkin, etc.—are scarcely mentioned in this book, but the elegant diffraction work of Hosemann and Renninger is given considerable prominence.

It is sad to think that Laue's death in an accident has withdrawn the founder of the subject from among us and that he will not be present next year at the fiftieth anniversary celebrations of his great idea in Munich. This book will serve as a constant memorial to him. H. Lipson

Modern Physics

By M. S. Smith. Pp. ix+254. (London : Longmans, Green and Co., Ltd., 1960.) 15*s*. net.

THIS is a lively and well-written account of the way physics has developed in the past sixty or seventy years. The author has a refreshingly original style and has attempted to convey the spirit of the investigations he describes as well as the essential detail ; he has avoided the rather dreary repetition of standard diagrams and tables that so many text-books adopt.

He is, however, rather unrealistic in claiming that it will serve as an introduction to the subject for sixth formers and undergraduates ; it can scarcely yet be claimed, for example, that a detailed consideration of Schroedinger's equation is merely introductory. The book is much more likely to be useful to the more mature physicist who wishes to have a readable survey of atomic and nuclear physics and who may wish to have some help in straightening out his ideas for presentation to others.

Moreover, the book scarcely justifies its title ; it contains nothing of solid-state physics, biophysics or modern developments in optics. Admittedly a book of this size and modest cost could not be expected to be so general, but the title ought to have been more specific.

The book is attractively produced and misprints and mistakes seem to be few. But it was copper sulphate, not zinc sulphide, that was first used to diffract X-rays (p. 40) ; the field of a dipole is inverse cube, not inverse fourth-power (p. 72) ; and the word 'anticipate' is incorrectly used on p. 80. H. Lipson

Laboratory Management and Techniques

By J. A. Edwards. Pp. xvi+207. (London : Butterworth and Co. (Publishers), Ltd., 1960.) 35*s*.

THE author makes clear in his introduction that this book does not pretend to deal with the higher problems of laboratory administration as this subject has been so adequately covered by E. S. Hiscocks in his excellent book (*Laboratory Administration*, London, 1956). A reading of Mr. Edwards' book, however, reveals that he too is dealing largely with administrative matters. The essential difference appears to be one of point of view. Mr. Edwards' conception of laboratory management is that of a laboratory steward. This conception is, in my opinion, better suited to the organization of teaching laboratories than to industrial and research laboratories. The value of the contents of the main part of the book

to all laboratories is nevertheless indisputable and quite independent of the organization-level from which it is viewed. There are six parts to the book, dealing with the new laboratory, laboratory organization and maintenance, accident precautions, special and auxiliary units, purchases and records, and staff problems and human relations. These parts are subdivided and filled with information and advice on design, organization, equipment and documentation. This information and advice is of a kind which is obviously based on a wide experience of practical laboratory management and has rarely been recorded in an accessible form.

Stores organization and fire precautions are particularly well dealt with. The special and auxiliary units include the radioactive materials laboratory, lecture theatre, photographic processes, workshops and library.

Those who occasionally import apparatus or chemicals will welcome the chapter on Customs and Excise procedures. This chapter deals also with applications for industrial methylated spirit, duty-free spirit and permission to use stills. It is admirably concise and informative.

The book is well produced and illustrated. It will be of great value to all whose duties include the provision of the ways and means of scientific endeavour.

E. I. JOHNSON

Lehrbuch der Organischen Chemie

13, neubearbeitete und erweiterte Auflage. Von Prof. Paul Karrer. Pp. xx+1080. (Stuttgart: Georg Thieme Verlag, 1959.) 60 D.M.

ORGANIC chemistry has undergone a great transformation both in extent and depth since Prof. Karrer's classic text-book first appeared in 1927, and much of this change has come about during the ten years that separate the last English from the new German edition of this work. Prof. Karrer has given recognition to this fact by inviting a group of authorities to revise and enlarge the existing text and to contribute a number of new chapters. The general layout and the major portion of the contents, however, remain unaltered.

While some of the newly written chapters, as, for example, those on conformational analysis, steroids, and amino-acids and polypeptides, are excellent, the shorter sections inserted into the old text are generally not well assimilated so that a consistent presentation fails to emerge. In particular the treatment of reaction mechanisms leaves an unsatisfactory impression. Throughout the book they are presented without formal consistency and the basis for their inclusion or omission is not readily apparent; alternative mechanisms are listed uncritically (Cannizzaro reaction, pinacol rearrangement, aldol condensation) and some are of an unorthodox nature (ester saponification, hemiacetal formation). Two further points of criticism force themselves on the reader's attention. A good deal of up-to-date information has been included, but at times abbreviated to an extent which obscures its significance (chemistry of caryophyllene, biogenetic role of phenol dehydrogenations). On the other hand, there are some surprising omissions (mechanism of halogen and halogen acid addition to olefins, Michael addition, Bredt's rule).

Prof. Karrer's book has for many years occupied a leading place among the text-books of organic chemistry. Its principal virtue still lies in the generous amount of factual information to be found within its covers, but one wonders whether its value as a pedagogic text can be effectively maintained by the method that has been adopted in this latest edition.

K. H. OVERTON

Radiation: Use and Control in Industrial Application

By Charles Wesley Shilling. (Modern Monographs in Industrial Medicine, Vol. 5.) Pp. viii+223. (New York and London: Grune and Stratton, Inc., 1960.) 6.75 dollars.

IN his preface, Dr. Shilling emphasizes that this book is non-technical and is intended for the person who needs only a working knowledge of the subject; in particular "the physician who must handle radiation exposure and injury cases and who must answer questions concerning the mysteries of radiation". In consequence the book has been written with a medical bias, but the author's aims have not been achieved since the treatment of the physical aspects of protection, such as shielding, instrumentation and monitoring techniques, is meagre and rather inadequate.

The first section of the book covers the origin and nature of the radiations and the dose to man due to natural sources, and is followed by sections on the prevention and treatment of radiation injury, the control of radiation and the use of radioisotopes. Although the treatment of each topic is, of necessity, concise, the subject-matter on the medical aspects is sufficient to acquaint the industrial physician with the various problems and to provide a basis for further reading. It should be noted, however, that the control procedures are considered from the United States point of view, and British readers should acquaint themselves with the national legislation and recommendations.

Some of the illustrations appear unnecessarily elementary and there are one or two errors in the text; for example, the maximum permissible concentration of radionuclides in air and water for the exposure of the entire population is given as one-tenth of the occupational exposure-level, whereas for individuals the International Commission on Radiological Protection recommends a reduction factor of one hundred. However, these errors are not serious provided the book is used for general reading rather than as a text-book.

B. E. JONES

Commutative Algebra

Vol. 2. By Prof. Oscar Zariski and Prof. Pierre Samuel. (The University Series in Higher Mathematics.) Pp. x+414. (Princeton, N.J.: D. Van Nostrand Company, Inc.; London: D. Van Nostrand Company, Ltd., 1960.) 58*s*. 6*d*.

THE first volume of this work was published in 1958. Now that the second volume has appeared it is possible to be much clearer on the motivation behind the subject as a whole. This is buried in the history of algebraic geometry, and the authors have been careful to indicate what parts of geometry have led to the immense algebraic developments of recent years. The book is very carefully written and will be an essential reference, and even a text-book, for the pure mathematician who moves or wishes to move in this field.

There are three long chapters, given to valuation theory, polynomial and power series rings and local algebra. In addition there is an appendix of about eighty pages containing a good deal of previously unpublished material. The contents of the chapter

on valuation theory are illustrated largely by examples from the theory of algebraic function fields; and the notions of normal and derived normal models, of great importance in geometry, are introduced. Geometry is seriously introduced in the chapter on rings, and includes an account of algebraic varieties in affine and projective space, together with a treatment of dimension theory, the Hilbert characteristic function and chains of syzygies. The chapter on local algebra gives an account of local rings and their properties, and then makes use of these rings in the local study of algebraic and analytical varieties. This study culminates in a section on analytical irreducibility and analytical normality of normal varieties.

This volume, together with its predecessor, is abstract from cover to cover. But the exposition is not condensed, and the work is likely to become the standard introduction to the arithmetic foundations of algebraic geometry. For this reason it seems a pity that, apart from a few scattered references, there is no bibliography. L. S. Goddard

Reciprocals of the Integers from 1000 to 9999, with an Appendix on Mechanical Barrel-setting Calculators

By T. H. Redding. Pp. iv+42+2 plates. (London: Taylor and Francis, Ltd., 1960.) 18*s.* 6*d.* net.

THE actual entries are the reciprocals to six figures, multiplied by 10^6, so that each entry is divided into two blocks of three digits by the decimal point, thus facilitating transfer from table to machine. The author does not say much about how the calculations have been checked, but some small sampling has revealed no error. There are no horizontal rules except in the frame, so the page is fairly clean, with 1,000 entries at an opening and a thumb-index. A clear modern 'equal height' fount is used, though it is scarcely as effective as the old-style 'head and tail' fount used by Comrie and Peters. There is an appendix of some twenty pages, in which the nature and use of barrel-setting desk machines are described in simple terms for the novice. The book should be of most value to those who are not expert at computation but have need now and then to make desk calculations. T. A. A. Broadbent

An Introduction to the Theory of Numbers

By Prof. Ivan Niven and Prof. Herbert S. Zuckerman. Pp. viii+250. (New York and London: John Wiley and Sons, Inc., 1960.) 6.25 dollars; 50*s.*

THIS compact and lucid text could be used by good sixth-form specialists or first-year honours students. In the first part of the book the basic concepts and theorems are presented: divisibility, primes, congruences, quadratic reciprocity, number-theoretic functions, diophantine equations, Farey series and continued fractions, the simpler properties of the distribution of the primes. The last three chapters introduce more specialized topics: algebraic numbers and number fields, the partition functions with the formulæ of Euler and Jacobi, and the fairly recent study of the density functions of a sequence of integers. The proofs are clear and concise, but they rightly demand a certain sophistication of outlook without which the reader is unlikely to be able to see why a particular line of argument is chosen. An excellent feature is the supply of exercises for the student; these range from simple corollaries on the main text to quite searching extensions of it; answers are given where appropriate. A young student with a taste for number theory and a firm grasp of elementary algebra would find the book profitable reading.

Elementary Logic of Science and Mathematics

By Dr. P. H. Nidditch. Pp. vii+371. (London: University Tutorial Press, Ltd., 1960.) 18*s.*

THIS book has two aims: to provide a detailed but elementary course in modern logic and to present basic material in the philosophy of science, covering probability and measurement, the scientific method and the construction of theories. The author has succeeded well in writing a book that is both accurate, informative and easy to read. About one-third of the book deals with formal logic; sentence logic is studied by means of a valuation theory (truth tables), and in terms of axiom systems. The predicate calculus is developed both as an axiomatic system and as a Gentzen-type system of natural inference; some attempt is made to wed the two codifications but a full equivalence proof is wanting. Among other axiom systems presented are Boolean algebra and a theory of probability. Definitions are given with great care, there are numerous historical references and a good collection of examples, with solutions or hints for solution.

The method used in the second part of the book is largely that of judicious quotation; the great scientists are allowed to speak for themselves and there is no attempt at criticism or comparative study, but there is a valuable selection from original sources.

R. L. Goodstein

Health in Industry

A Guide for Engineers, Executives and Doctors. By Prof. R. C. Browne. Pp. vii+157. (London: Edward Arnold (Publishers), Ltd., 1961.) 18*s.* net.

OVER the years the Nuffield professor of industrial health at King's College, Newcastle upon Tyne, has delivered courses of lectures to science, medical and technological students at the University on various aspects of occupational health. The subjects have been varied and topical, and have shown concern for the health of the executive, the heavy cost of sickness absence, the importance of good design, the causes and consequences of accidents and fatigue, automatic processes and their effects on the worker and the part played by good working conditions on output. Particular attention is directed to the essential precautions which must be taken in using ionizing radiations, while Prof. Browne also analyses the influence of various chemical substances on the factory worker.

The author has now addressed his lecture-material to all employers and managers who are, in some way or other, responsible for the industrial environment. Much of it will be of interest and value, and the book should appeal to many who bear responsibility for people in industry. The book could also be used in industrial health sessions during courses on industrial administration. In such a book a surprising feature is the absence of all reference to skin diseases and the use of barrier creams which may cause more complaints than they cure. In the section on the health of the manager, the author might also have given some practical advice about diet. Many industrial executives become ill because they are unaware of the simple rules of health, although they sometimes call their complaint 'pressure of work'. T. H. Hawkins

LETTERS TO THE EDITORS

SEISMOLOGY

Microbarograph Records from the Russian Large Nuclear Explosions

DURING the recent series of Russian atomic weapon tests, microbarographs were operated at this Establishment. The instruments used were purely mechanical devices having limited frequency response. Excellent records were obtained from several of the larger firings at Novaya Zemlya and particularly from the 50-megaton firing of October 30. Taking the origin time as 08.33 hr. from a study of the seismic signal, we saw the start of the first characteristic microbarograph record (Fig. 1*a*) 3 hr. 11 min. later at 11.44 hr. on October 30; subsequent to this, we obtained clear signals at approximately 16.40 hr. on October 31 (Fig. 1*b*); 00.10 hr. on November 1 (Fig. 1*c*); and 12.40 hr. on November 2 (Fig. 1*e*). We looked for a signal at around 05.10 hr. on November 2 but could not see one against the background (Fig. 1*d*).

It would appear that the waves are being successively reflected at the antipodes of Novaya Zemlya and at Novaya Zemlya, with relatively little absorption or scattering. We have re-examined our records of the 30 megaton firing on October 23 and they show similar evidence of reflexions corresponding relatively in time to those shown in Figs. 1*b* and *c* for the 50-megaton firing, but with the signal to noise ratio much smaller.

Observations made on the phenomena with more refined instruments or arrays and a compilation of results on a world-wide scale could yield extremely interesting data about the Earth's atmosphere. We have noticed a number of points of interest already in our brief examination of the records. For example, there is a good agreement between the wave shape observed and the form one would expect from a study of the paper by Hunt *et al.* (ref. 1, particularly Fig. 10). Brune *et al.*[2] have recently treated the problem of an elastic surface wave on a sphere and found a $\pi/2$ phase shift at each polar reflexion; our observations, although difficult of interpretation because of dispersion, do suggest a phase reversal after two such reflexions. The waves diverging from the origin (Figs. 1*a*, *c* and *e*) also appear to have a simpler, more compact, waveform than the waves converging on to the origin (Fig. 1*b*).

An interesting comparison can also be made with the records obtained following the eruption of Krakatoa in 1883[3]. The average time along several paths for waves to pass around Earth following Krakatoa was 36 hr. 20 min. ± 10 min. (*S.E.* 35 readings), the corresponding figure from our records being 36¼ hr. 27 min. with an accuracy of a few minutes.

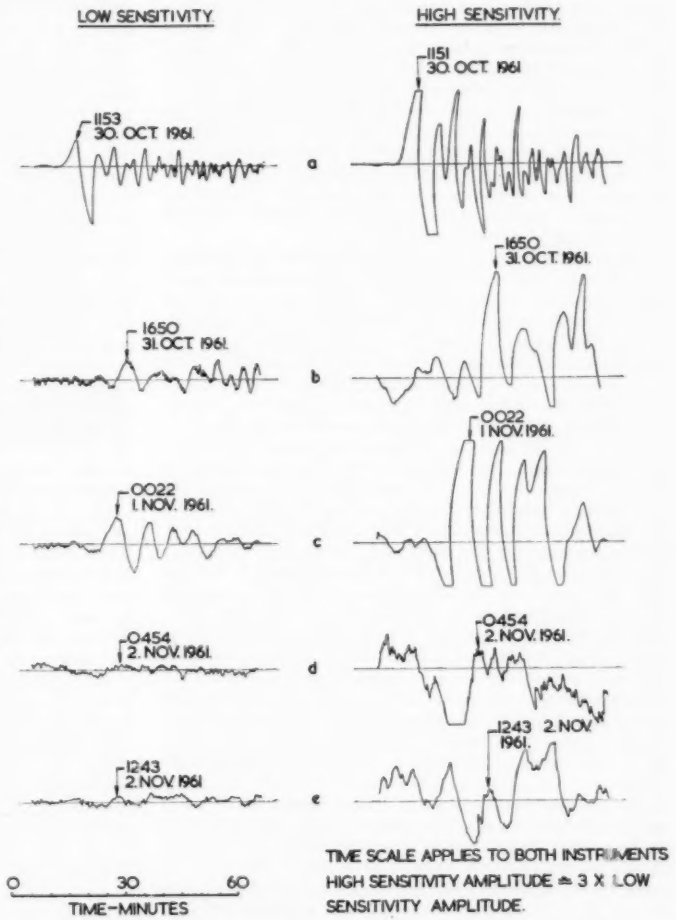

Fig. 1. Microbarograph records taken at the Atomic Weapons Research Establishment, Foulness

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ASTRONOMY

The Galactic Red Shift

The recent development of the technique of resonant scattering of γ-rays, using the Mössbauer effect, appears to raise the possibility of a terrestrial test of one theory of the red shift observed by Hubble in the light coming from distant galaxies.

The usual interpretation of the galactic red shift is that it is a Doppler effect due to mutual recession of the centres of the galaxies; there are, however, other possible interpretations, and among these is the suggestion by Finlay-Freundlich[1] that it is due to loss of energy by light in passage through a radiation field. Finlay-Freundlich was led to this conclusion from a study of stellar red shifts and put forward the empirical relation that the fractional energy loss is proportional to the path-length and the fourth power of the temperature (energy density) of the radiation field. With this simple empirical relation and using the observed stellar and galactic red shifts, he deduced a value for the average intergalactic (radiation) temperature which does not seem unreasonable on general thermodynamic grounds.

Born[2] pointed out that Finlay-Freundlich's empirical relation might correspond to an otherwise unknown photon–photon interaction in which loss of energy occurs without change in direction of the photon. Born showed that there was some evidence in the empirical relation for a fundamental length which ought perhaps to be part of a general description of the radiation field, and suggested that the energy apparently lost might reappear as radio emission.

These suggestions by Finlay-Freundlich and Born, if correct, would have very far-reaching consequences in cosmology and in the field theory of elementary particles. However, several authors[3] have directed attention to certain difficulties. Among other points, it is asserted that the observed stellar radio emission and the change in red shift of binary stars in eclipse are too small to be consistent with the proposed theory. Some of these difficulties may be very real, but bearing in mind the experimental difficulties in measuring stellar red shifts, the variety of causes which can result in both red and blue shifts, and that an otherwise unknown photon–photon interaction could result in the appearance of an entirely unknown particle, it seems worth considering the possibility of a terrestrial experiment under controlled conditions.

At present, attempts are being made at Harwell and elsewhere to observe the gravitational red shift using γ-rays from iron-57 and the Mössbauer effect. The resolution using iron-57 is $\sim 6 \times 10^{-13}$. It is easy to show that if the γ-rays in these experiments were allowed to pass through a radiation field of similar quality and the same order in energy density as on the surface of the Sun, extending over a distance of about a metre, the red shift expected from Finlay-Freundlich's relation is about 1 per cent of the resolution. 1 per cent is not far from the expected gravitational red shifts in the present experiments in which the photons fall considerably larger distances. In a practical attempt to test Finlay-Freundlich's relation, it would probably be necessary to have a radiation density times path-length such that the expected shift would be of the same order as the resolution; and although this would require a considerable effort, it does not seem entirely beyond present pulse techniques such as are used in thermonuclear work, but in this case involving lower plasma temperatures. It should be a reasonably fair test if most of the energy in the radiation field lies in or near the visible region, and if the dependence on energy of the incident photon in Hubble's law can be regarded as sufficiently well established.

A negative result for this proposed experiment would serve the useful purpose of removing one theory of the galactic red shift. At present it would be idle to pursue in detail the various possible interpretations of an unambiguous positive result, but it may be of interest to outline one of these briefly and simply here.

If we can regard our Sun as typical of about 10^{11} stars in a typical galaxy and use a value of $\sim 2 \times 10^{9}$ light years as the average intergalactic distance, it is easily shown that the average rate R_1 of release of radiation into unit volume of intergalactic space is $\sim 3 \times 10^{-33}$ erg/c.c./sec. The average rate R_2 of apparent loss of energy by photons in the galactic red shift is $K\rho$, where K is Hubble's empirical constant and ρ is the average energy density of radiation in intergalactic space. Using a value for K of 5×10^{-18} sec.$^{-1}$ and for ρ of $\sim 6 \times 10^{-13}$ erg/c.c., it is clear that $R_1 \sim R_2$. Confirmation of Finlay-Freundlich's relation would justify this value of ρ and also the qualitative interpretation $R_2 = K\rho$. In these circumstances the galactic red shift becomes a vast sink which receives the radiation from the stars and transforms it into some other form, the processes involved being in approximate equilibrium at present. It does not seem entirely inconceivable that at least some of the energy thus transformed might reappear eventually in space as neutrons by a net reaction involving unknown particles. The hydrogen from the neutron decay would provide fuel for new stars as in Hoyle's theory of continuous creation. The net effect of the entire process would be to slow up what seems at present an inevitable decline towards a universe of black dwarfs, photons and neutrinos as the hydrogen in the stars is steadily transformed to helium photons and neutrinos. The amount of recycling of hydrogen by such a hypothetical process could be quite large, as most of the energy released in the net reactions in the stars goes to the photons which escape from the stellar surfaces. Approximate equilibrium at present need not conflict, at least qualitatively, with the recent results of Ryle, if a 'beginning' consisting of a vast hydrogenous cloud is assumed, for in the early stages of condensation the low value of ρ would correspond now to an apparent increase in the frequency of observation of low-intensity (assumed distant) sources.

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OCEANOGRAPHY

Ultra-violet Absorption of Sea Water

It has been shown that at wave-lengths less than 230 mμ., the absorbency of sea water is about double that of a solution containing the same concentration of inorganic salts[1,2]. We ascribe the difference to the

presence of organic matter which may be the same as the blue-absorbent substances named "Gelbstoff" by Kalle[3]. We have found regional differences in the east Atlantic and English Channel, high ultra-violet absorbencies usually being characteristic of coastal water[2]. This property may be used in hydrographic surveys, and for this purpose we have measured the absorbencies of filtered samples at 220 mμ, using a 10-cm. cuvette in a Unicam *S.P.*500 spectrophotometer.

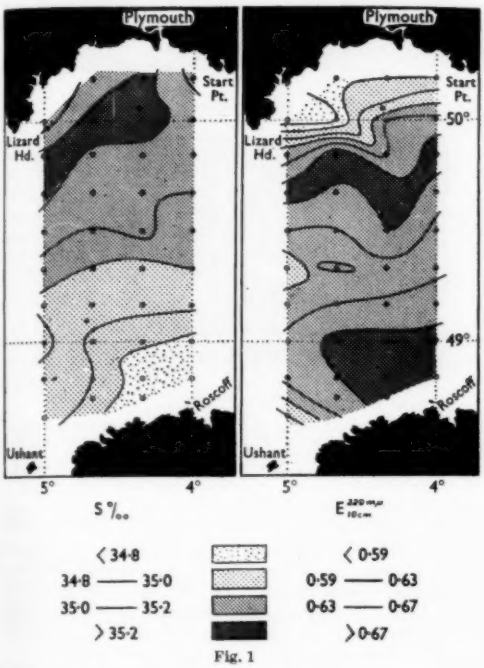

Fig. 1

Ultra-violet absorbencies of samples from 10 m. depth from a survey across the English Channel in April, 1961, are compared with salinities in Fig. 1. Water of low salinity and high ultra-violet absorption was found in the south-east corner of the area, and has presumably come down Channel on the French side, being diluted with land drainage. On the English side there is an intrusion from the west of higher salinity water of low ultra-violet absorption which we think is of Atlantic origin. This water appears to have displaced water of salinity 35·1–35·2 per mille but of higher ultra-violet absorption (E(200 mμ, 10 cm.) approx. 0·7) which was found off Plymouth in February, 1961 [2]. This displaced water, though indistinguishable by its salinity, is made evident as a band of high ultra-violet absorption in mid-Channel.

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PHYSICS

Proposed Harmonic Generator or Mixer for Optical Frequencies

In a recent communication[1], Lainé has suggested the use of my latest form of 'cold cathode' arc harmonic generator as a mixer for obtaining beats at high microwave frequencies (that is, frequencies corresponding to submillimetre waves) between the outputs from two optical masers. I would like to comment on this proposal and suggest a simpler alternative device.

If one accepts the principle of field emission as the source of electrons from the cathode of the arc harmonic generator, then Lainé's suggestion is indeed feasible. On this basis one calculates that for the liquid platinum cathode used at present, the electron emission current density must be about 10^8 amp./cm.^{2} for a cathode spot diameter of about 1μ. The positive ion field required to produce this emission must be of the order of 10^8 volts/cm., extending over a region of only 10 Å. outwards from the cathode surface. The time-constant of the electron emission process should thus not exceed 10^{-15} sec. If the outputs from the two optical masers were first plane-polarized with the electric vectors perpendicular to the cathode surface and then focused into a region one optical wave-length in diameter (at glancing incidence) at the cathode spot then the positive ion space-charge field would have a superimposed field at optical frequencies and the electron emission should vary at the beat frequency. To produce a reasonable effect, optical fields in excess of 3×10^7 V./cm. would be required—implying maser powers of tens of kilowatts. A second disadvantage is that microwave conduction along the arc plasma (the only means of communication with the cathode spot) is shunted by diffusion spreading of the plasma in the region of the cathode, thereby imposing an upper limit to the beat frequency which can be detected. For the argon plasma at 300 atmospheres pressure this limit is about 700 Gc./s.

However, a possible field emission mixer can be made very simply. All that is required is a small drop of liquid cæsium in a glass vacuum enclosure. The energy from the optical masers should be plane polarized with the electric field perpendicular to the cæsium surface and focused into a spot about 1μ diameter striking the cæsium at glancing incidence. Strong field emission would take place for field strengths of 10^7 V./cm. which could be obtained with 3 kW. of maser power. The optical waves would penetrate the liquid surface to a depth more than an order of magnitude greater than that needed to overcome the potential barrier. During the positive going half-cycle of the optical electric field, electrons would thus be emitted in a highly 'non-linear' manner, travelling outwards for about 20 Å. in 10^{-15} sec. This oscillating charge would radiate at the beat frequency and at harmonics of the optical frequencies. As an optical frequency doubler, efficiencies approaching 1 per cent might be attained.

Further reduction of the maser power required for beat production should be possible if one makes use of the field emission studies of Martin, Trolan and Dyke[2]. They have drawn electron currents of several m.amp. continuously from a tungsten point of 0·1μ radius. If the maser output could be focused on to such an emitting point, the electron current would be modulated at the beat frequency. Some sort of magnetic focusing of the electron beam would be

necessary to prevent space-charge demodulation and to enable the energy in the electron bunches to be coupled to a microwave waveguide circuit. Beat frequencies in excess of 1,000 Gc./s. should be practicable by such a method.

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Detection of Spin Magnetization Variation in a Two-level Maser Oscillator

The phenomenon of amplitude modulation in the spontaneous emission of two-level masers has been observed by several investigators[1-3], and has been the subject of a number of theoretical discussions[3-5]. The basic mechanism underlying most of the semi-classical treatments is an oscillatory transfer of energy between the spin system, in the working substance, and the cavity radiation field. In such a process the spin magnetization vector M should undergo damped, pendulum-like nutations, correlated to the modulation of the emission, between the inverted state, M anti-parallel to the steady magnetic field in the z direction, and the thermal equilibrium state, M parallel to the steady field. The quantum mechanical treatment[6] of the interaction between the spin system and the radiation field in the cavity also suggests the oscillatory behaviour of M_z. Stevens[6] further suggested that the direct observation of the variation of M_z, during an oscillation pulse, would be a more instructive test of the theories mentioned than monitoring the modulated cavity energy. Evidence confirming the suggested behaviour of M has been obtained in an induction experiment designed to detect the variations in the 'dipole' field of M_z.

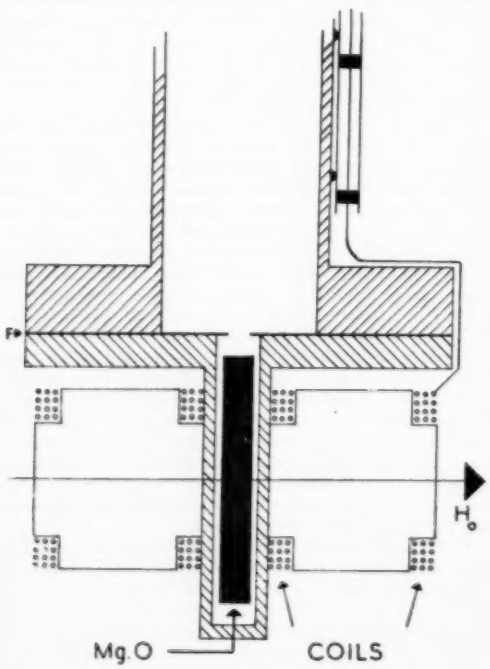

Fig. 1. Cavity with sample, pick-up coils and co-axial lead. Cavity, 0·9 × 0·1 × 0·8 in., sample, 17·5 × 2·0 mm. *F*, Silver-plated copper foil with iris to wave-guide

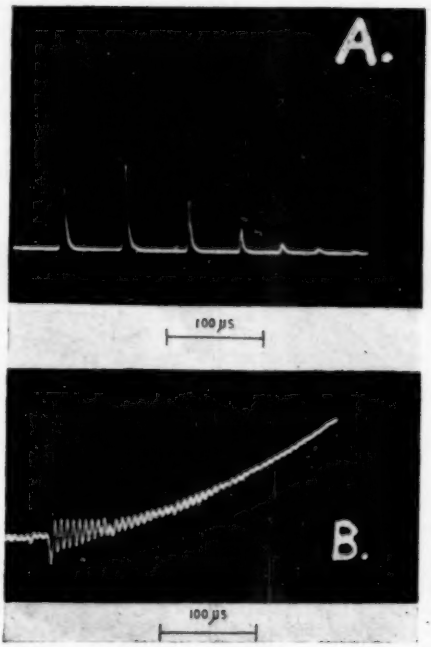

Fig. 2. *A*, Modulated emission from field-swept two-level maser: maximum power, 17 mW. *B*, Shock excitation of pick-up coils due to nutation of magnetic moment of the spin system; maximum pick-up voltage, 0·5 mV.

The maser operated in this laboratory[7] is of the field-swept type. The sample, neutron-irradiated magnesium oxide containing about 5×10^{18} spins, was mounted in a rectangular 'TE_{102}' plastic cavity resonator[8]. Oscillation pulses have been observed in which the amplitude modulation frequency was dependent upon the rate of field sweep. It was estimated that the skin-depth at these frequencies was greater, by orders of magnitude, than the cavity silver plating, so that variations of the field of M_z would not be totally confined within the cavity. Furthermore, calculations predicted that the voltage induced by this flux in an external coil, of 800 turns, surrounding the sample would be of the order of a millivolt.

Such a coil system should be balanced against pick-up from the swept field. The coil assembly used in this experiment satisfies this requirement, to a sufficient extent, and is shown in Fig. 1. The field of M_z would couple only to the inner coils, whereas the outer coils compensate for the pick-up of the swept field in the inner coils. At 1·2° K. the coils had a resonant frequency of 150 kc./s.; $Q = 4$ and a damping time constant of 60 μsec.

Maser oscillations and the corresponding pick-up voltage in the coils were simultaneously recorded on two oscilloscopes. Typical oscillograms of these recordings are shown in Figs. 2*A* and 2*B* respectively.

The oscillation envelope, shown in Fig. 2*A*, is not continuous so that variations of M_z should occur only during the intermittent pulses, leading to shock excitation of the pick-up coils. This was found to be advantageous because the response time of the system is too long to record completely the variations of M_z. In Fig. 2*B* there are shock excitations coincident with the first three oscillation pulses. This coincidence was checked in a special experiment. The rising baseline is due to the residual pick-up from the swept field. This evidence, in support of the nutating character of M, is further substantiated by the fact that no effect was observed when the inverting microwave power was reduced below the level necessary to sustain maser oscillations so that only the residual pick-up was observed.

This experiment establishes the existence of variations of M_z and therefore of the nutations of M during emission. Further measurements of M_z will, very likely, provide useful information on the mode of operation of maser oscillators. The technique described could be improved, to give detailed measurements of M_z, either by using critical damping in the pick-up coils, or by modifying the system to respond to the nutations of M as modulations of a high-frequency carrier wave fed to the coils.

We are indebted to Prof. J. F. Allen for placing low-temperature facilities at our disposal and to the Royal Naval Scientific Service for the interest shown in this work.

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GEOLOGY

Occurrence of Magnesite–Dolomite Sediments in South Australia

In November 1960 samples of precipitating sediment were taken from a lagoon of saline water near Salt Creek in the south-east province of South Australia. These were found to consist of magnesite and dolomite in about equal proportions. The salinity of the water was 3·2 per cent, and analysis showed that calcium constituted a much smaller proportion of the total salts than in normal sea-water. The proportion of magnesium was also lower. The *p*H was about 10.

Samples were taken from the bed of the lagoon after it had become dry during the summer. At the surface the proportions of magnesite and dolomite were approximately equal. At a depth of 6 in. the approximate composition was magnesite 20 per cent, dolomite 80 per cent. At 10 in., magnesite was no longer detectable and the sediment consisted entirely of dolomite. This persisted to a depth of 20 in., where it graded sharply into black sulphide-bearing sands.

X-ray examination of the magnesite showed that the lattice was expanded when compared with normal magnesite. The lattice constants were estimated as $a_0 = 4{\cdot}66$ and $c_0 = 15{\cdot}23$. This may be compared with the magnesium carbonate described by D. L. Graf, A. J. Eardley and N. F. Shimp[1] from Lake Bonneville, U.S.A., which has a significantly expanded unit cell with lattice constants $a_0 = 4{\cdot}669$ and $c_0 = 15{\cdot}21$.

Last year we[2] recorded the occurrence of hydromagnesite–aragonite sediments in a similarly situated lagoon which is about 8 miles south of the lagoon in which the magnesite–dolomite is forming. This new discovery may throw more light on the origin of the magnesite–dolomite sediments of Proterozoic age in South Australia.

We believe this to be the first recorded observation of naturally precipitating magnesite–dolomite sediment.

This work is supported by grants from the American Petroleum Institute.

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CRYSTALLOGRAPHY

X-ray Data for the Chrome-Urania System, $Cr_2O_3{\cdot}2UO_3$

A new binary compound in the chrome-urania system has been briefly described by Borchardt[1]. This compound has been prepared by mechanically mixing 78 weight per cent uranium oxide (UO_3) and 22 weight per cent chromium oxide (Cr_2O_3), pressing the mixture into pellets and firing to 1,250° C. in platinum dishes. The samples were reground and refired and then examined by chemical, optical, and X-ray techniques. A trace of free chrome was observed optically in mixtures where the chemical analysis indicated excess chromium over a Cr : U atom ratio of 1. The X-ray powder patterns indicated only one phase.

The preparations were black, with grain sizes less than 50μ. Two small crystals which were recovered from the preparations showed external morphology with $6/m$ symmetry. Single-crystal precession photographs, however, showed the crystals to be truly orthorhombic with three-fold interpenetrant twinning producing the pseudo-hexagonal habit. Fig. 1 shows the true orthorhombic lattice and its relation to the twin in the $0kl$ zone. Of particular interest is the superposition of the 002 and 041 reflexions. Table 1 lists the X-ray powder pattern along with the indexing based on the cell determined from the single-crystal patterns. Table 2 lists the cell data and optical properties of the compound.

The presence of the pseudo-hexagonal twinning suggested the possibility of a high-temperature inversion to a truly hexagonal phase. Using a hot-stage furnace (Materials Research Corporation), samples were examined in air up to 1,400° C., but no evidence for the expected phase change was found. However, samples left at 1,250° C. for several days developed clusters of multiple and single crystals of the compound on the surface of the sample. The crystals were yellow-brown tabular crystals with a rectangular outline. Most of the crystals were twinned, producing

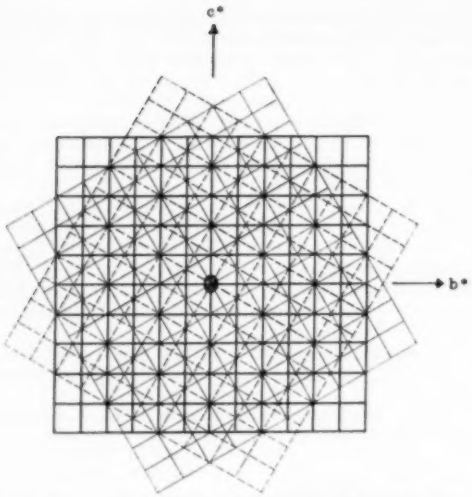

Fig. 1. Relationship of the true cell in the 0*kl* zone with respect to the twinned lattices. The true cell is shown as heavy lines. Only points with $k = 2n$ are included, since reflexions with $k = 2n + 1$ are extinct. Notice particularly the superposition of 041 and 002 in different lattices

a 'cockscomb' effect around the periphery of the plates.

Several crystals were examined with the precession camera. The twinning was the same as mentioned above. Untwinned crystals showed extinctions in *hk*0 when $h + k = 2n + 1$, *h*0*l* when $l = 2n + 1$, and 0*kl* when $k = 2n + 1$. Very weak reflexions are noted for *hkl* when $h + k = 2n + 1$, and *h*0*l* when $l = 2n + 1$. The extinctions indicate the unique space group *Pbcn* with a pseudo symmetry *Cmcm*. The specific gravity of the crystals is greater than 3·3, which suggests either one molecule per unit cell with a calculated specific gravity of 4·18 or two molecules with a specific gravity of 8·36. One molecule would produce a problem with respect to the position of the ninth oxygen in the unit, because the space group does not allow any odd-fold special positions. This inconsistency can indicate either that the oxygen is statistically distributed over 2-, 4-, or 8-fold sites, or the chemical analyses are incorrect in

Table 1. X-Ray Powder Pattern for $Cr_2O_3 \cdot 2UO_3$

hkl	$\sin^2\theta_{calc.}$	$\sin^2\theta_{obs.}$	*I*	*hkl*	$\sin^2\theta_{calc.}$	$\sin^2\theta_{obs.}$	*I*
020	0·0174	0·0174	vw	240	0·1700	0·1686	w
110	0·0295	0·0294	w	202	0·1931	0·1930	s
021	0·0405	0·0408	vw				
111	0·0526	0·0532	vs	241	0·1932		
130	0·0642	0·0643	s	222	0·2105	0·2105	vw
040	0·0694	0·0687	w	023	0·2255	0·2259	m
131	0·0873	0·0874	vw	310	0·2307	0·2308	vw
041	0·0926			?		0·2347	w
002	0·0925	0·0925	m	113	0·2377	0·2384	m
200	0·1006	0·1006	mw	170	0·2378		
022	0·1099	0·1108	w	062	0·2488	0·2474	w
220	0·1180	0·1179	w	311	0·2538	0·2535	m
112	0·1220	0·1225	w	260	0·2568	0·2579	m
150	0·1337	0·1323	m	330	0·2654	0·2640	m
221	0·1411	0·1412	ms	133	0·2724	0·2735	vw
060	0·1562			043	0·2776		
132	0·1567	0·1567	s			0·2778	m
151	0·1568			080	0·2778		
042	0·1620	0·1614	w	081	0·3009	0·2974	m

Table 2 X-Ray and Optical Data for $Cr_2O_3 \cdot 2UO_3$

a_0 = 4·857 ± 10 Å. $\rho_{calc.}$ = 8·36 gm./c.c.
b_0 = 11·692 ± 10 Å. Colour = golden brown
c_0 = 5·074 ± 10 Å. $Nx > 2{\cdot}11$
V = 288·0 Å.^{3} $Ny > 2{\cdot}11$
Z = 2 $Nz > 2{\cdot}11$

We thank Dr. J. S. Kahn, of this Laboratory, for the optical data.

indicating a fully oxidized uranium. The specific gravity of 8·36 is reasonable when compared with specific gravities of the components. Using Vegard's law and values of 5·24 and 8·24 for Cr_2O_3 and UO_3 respectively, the calculated specific gravity for 80 weight per cent UO_3 and 20 weight per cent Cr_2O_3 is 7·64. Because deviations from Vegard's law would tend toward smaller unit-cell dimensions and high specific gravities, the values of 8·36 for two molecules per unit cell is acceptable.

Single-crystal intensity data are now being collected for determination of the crystal structure.

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Structure of Asparagine Monohydrate

The structure of asparagine has been discussed several times during recent years[1–5]. A number of properties would be better explained by a ring structure than by the conventional straight-chain structure[1,2], but on the other hand, the carboxylic group had to be free[3]. The structure of crystalline asparagine monohydrate has now been determined by us with X-rays, and although this does not give definite information about the structure of the molecule in solution, it does give some indications about it.

Table 1. Atomic Co-ordinates (Å.)*

	y	*z*	*x*
C_1	4·888	9·247	0·421
C_2	3·867	9·549	1·529
C_3	4·404	0·563	2·679
C_4	0·097	9·795	3·294
N_1	3·257	8·272	2·029
N_2	0·584	0·629	4·344
O_1	5·554	0·428	0·008
O_2	4·916	8·091	11·747
O_3	0·621	8·773	2·818
O_4	1·695	2·258	1·319

* With the origin halfway between three pairs of non-intersecting screw axes.

The molecules in the crystal appear to be held lightly together by several hydrogen bonds, as could be expected (Fig. 1 and Table 2). First of all, there is a continuous spiral of hydrogen bonds, in the direction of the *a* axis, involving the water molecules (O_4) and the double-bonded oxygens of the carboxylic groups (O_1). Then there are three hydrogen bonds linking the nitrogen of the amino group (N_1) with different oxygen atoms: O_3 (in another molecule), O_4 and O_2. The nitrogen of the amido group (N_2) forms only one good hydrogen bond, with O_1; the other one, with O_2, is weaker.

Of interest in connexion with the discussion whether the structure of asparagine is a ring or an

Table 2. Interatomic Distances (Å.)

Covalent bonds		Hydrogen bonds	
$C_1 - O_1$	1·27	$O_4 - O_2$	2·84
$C_1 - O_2$	1·34	$O_4 - O'_1$	2·80
$C_1 - C_2$	1·54	$N_1 - O'_1$	2·80
$C_2 - N_1$	1·50	$N_1 - O'_3$	2·81
$C_2 - C_3$	1·51	$N_1 - O'_4$	2·85
$C_3 - C_4$	1·53	$N_2 - O'_1$	2·92
$C_4 - O_3$	1·24		
$C_4 - N_2$	1·33		

A prime indicates an atom from a different molecule.

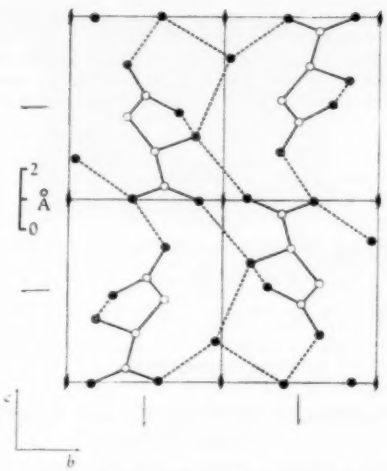

Fig. 1. Arrangement of the molecules of asparagine and water in the unit cell, as seen along the *a* axis; origin on two-fold screw axis parallel to the *a* axis. Covalent bonds and the hydrogen bonds ≤ 3·0 Å. are shown. ○, Carbon ●, nitrogen; ●, oxygen

open chain is the question whether there is some kind of a bond between N_1 and O_3 atoms of the same molecule. The distance between N_1 and O_3 within the same molecule is rather short (3·09 Å.), but the distances between N_1 and three other oxygen atoms are still shorter (Table 2). Moreover, the difference Fourier shows hydrogen atoms in correct positions for hydrogen bonds between those atoms, but nothing between N_1 and O_3 atoms of the same molecule. Therefore, it can be concluded that there is no intramolecular hydrogen bond between N_1 and O_3 in crystalline asparagine. However, this does not rule out the possibility of a hydrogen bond in this position in solution. The structure would then be a kind of intermediate between a ring and a chain and so could account for all properties. The ring, for example, looks like the ring in proline and could therefore explain why asparagine reacts with ninhydrin in the same way as proline, and not as the other amino-acids, including glutamine[1,2].

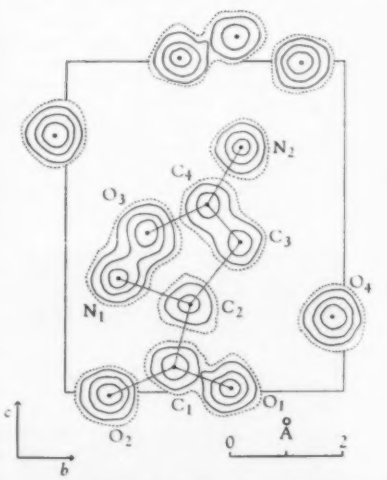

Fig. 2. Fourier projection of asparagine monohydrate on the (0yz) plane, after two cycles of refinement of the *y* and *z* co-ordinates. Origin as in Fig. 1

Crystallographical data about the structure are: space group $P2_12_12_1$, $a = 5{\cdot}582$ Å., $b = 9{\cdot}812$ Å., $c = 11{\cdot}796$ Å., unit cell volume = 646·1 Å.^{3}, four molecules per unit cell. $D_0 = 1{\cdot}543$ gm./cm.^{3} (ref. 6), $D_x = 1{\cdot}543$ gm./cm.^{3}.

The structure was solved using the three-dimensional sharpened Patterson. The *y* and *z* co-ordinates were first refined using the Fourier projection on (0*yz*), after two cycles giving an *R* factor of 16·2 per cent and the Fourier projection represented in Fig. 2. Then all the co-ordinates and the anisotropic temperature factors were refined using least squares programmes on the *IBM* 704. The final *R* value was 7·4 per cent.

The final atomic co-ordinates are shown in Table 1; the intra-molecular bond-lengths and the hydrogen bond-lengths ≤ 3·0 Å. are shown in Table 2: these hydrogen bonds are also shown in Fig. 1. Other distances between nitrogen and oxygen shorter than 3·25 Å. are N_2–O_2 = 3·02 Å. and N_1–O_2 (intramolecular) = 3·09 Å. There were no intermolecular distances involving carbon atoms shorter than 3·3 Å.

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Crystal Structure of 2-Phenylazulene

AFTER a long controversy, the space group of azulene is now apparently established as the centrosymmetric $P2_1/a$, with two non-centro-symmetric molecules in the unit cell[1,2], a result which leads to a disordered structure in which successive azulene molecules in the crystal are reversed in direction at random. Two previously observed cases of random positioning, namely, between chlorine and bromine in *p*-chlorobromobenzene[3] and between methyl and chlorine in 2-amino-4-methyl-6-chloropyrimidine[4], involve atoms or groups of comparable size, and are not as surprising as is the case of azulene, where there is a rather large difference in size between the five- and seven-membered rings.

The disorder in the azulene structure complicates the precise determination of the bond-lengths in this interesting molecule. Accordingly we initiated an X-ray study of a derivative, 2-phenylazulene. Crystals of this substance were found to be monoclinic, with $a = 7{\cdot}92 \pm 0{\cdot}02$, $b = 5{\cdot}79 \pm 0{\cdot}03$, $c = 11{\cdot}81 \pm 0{\cdot}02$ Å., $\beta = 90°$. The observed density is $1{\cdot}24_8$ gm./cm.^{3}; the density calculated for two molecules per unit cells is 1·252 gm./cm.^{3}. Weissenberg photographs taken about the three principal axes showed the absences (*h*0*l*) with *h* odd and (0*k*0) with *k* odd. The space group is therefore also $P2_1/a$. The lattice constants of azulene itself are[1] $a = 7{\cdot}91$, $b = 6{\cdot}00$, $c = 7{\cdot}84$ Å., $\beta = 101° 30'$, and it may be noted that the values of *a* and *b* are quite similar for

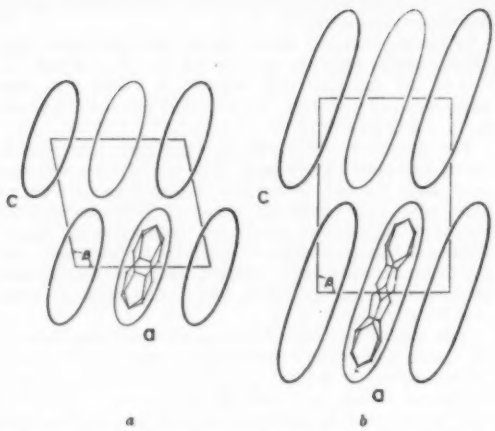

Fig. 1. The unit cells of azulene (*a*) and 2-phenylazulene (*b*)

both crystals. In the azulene structure, the long axis of the molecule lies very close to the direction [102]. If the molecule is now lengthened by the substitution of a phenyl group in the 2 position while at the same time preserving the relation between adjacent molecules as found in azulene, then the unit cell of 2-phenylazulene is reproduced very closely. In the broad sense, then, the two structures are isotypic, as may be seen in Fig. 1, which shows the close relationship between the two unit cells.

A trial structure for 2-phenylazulene was formulated on the basis of the above assumptions, and after trial and error adjustments the Fourier transform of two superimposed molecules yielded satisfying agreement with the observed values of F_{A0l}. The electron density projected down *b*, as calculated with 48 of the 72 observed F_{A0l} together with the signs obtained from the transform, is shown in Fig. 2.

These considerations strongly imply that the structure of 2-phenylazulene, like that of azulene, is disordered, with the direction of the long molecular axis reversed at random. A disordered structure for azulene is unexpected, but a similar structure for the 2-phenyl derivative seems even more unexpected since it suggests that the two ends of the molecule are essentially indistinguishable during the crystallization process. Additional refinement of the structure is proceeding.

We wish to thank Prof. E. Heilbronner for excellent crystals of pure 2-phenylazulene. This work was supported by the U.S. National Science Foundation.

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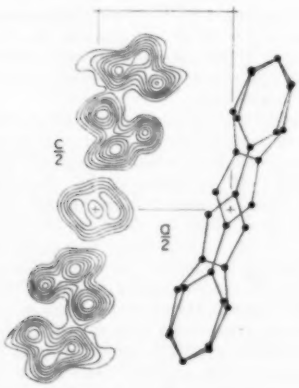

Fig. 2. Projection of the 2-phenylazulene structure on (010)

CHEMISTRY

Preparation of Single-Crystal Graphite from Melts

Single-crystal graphite demonstrates a very high degree of anisotropy between the properties obtained in directions parallel and normal to the basal plane. This has generated a great deal of scientific curiosity. The closest approach to single-crystal graphite so far has been in the purification and recovery of flakes of natural graphite. Unfortunately, the flakes of natural graphite are imperfect; well-developed single crystals are rather scarce, especially in the larger sizes. It is felt that the following technique for producing single-crystal graphite will provide basic material for work on carbon and graphite and for optical work requiring single-crystal lamellæ.

We have been successful in producing single-crystal graphite by heating in a graphite crucible some titanium boride powder at 2,500° C. under vacuum for 2 hr. A thin, highly reflecting, flexible film forms at the surface of the melt, which may then be carefully removed from the substrate (Fig. 1). Alternatively, single-crystal graphite films can be produced in graphite crucibles on the surface of melts of tungsten, zirconium carbide, nickel, chromium, rhenium and molybdenum, heated at the proper temperatures.

Results from X-ray diffraction of the films indicate that the material possesses the highest degree of orientation, having lattice spacings identical with the classical values given in the literature. Electron diffraction observations (Fig. 2) and electron optical investigations confirm the single crystallinity of the material (ref. 1 and personal communication between T. H. Johnson and H. Fernandez-Moran).

The mechanism of the technique described for graphite single-crystal growth is undoubtedly different from that in the decomposition of aluminium carbide[1];

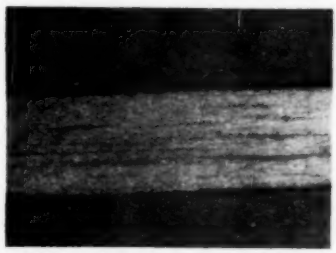

Fig. 1. Cross-section of single-crystal graphite. (× 500)

Fig. 2. Reflexion electron diffraction pattern of single-crystal graphite (Radio Corporation of America *EML*-1 electron microscope, at 50 kV. electrons and 50 cm. distance)

in the present instance, the growth may be attributed to the formation of supersaturated solutions of carbon in the melt. A detailed investigation of the mechanism in the present technique for graphite growth has begun.

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Definition of Rate Constant and Activation Energy in Solid State Reactions

DISLOCATIONS in alkali halide crystals doped with silver ions can be 'decorated' by a hydrogen treatment, which causes reduction and subsequent precipitation of silver[1]. In the course of work on the kinetics of this solid state reaction, the problem arose of deducing the reaction constant and the activation energy without exact knowledge of the reaction mechanism, which is rarely discussed in the literature.

The definition of a rate constant k and an activation energy E for solid state reactions in analogy with reactions taking place in gases or solutions gives rise to several difficulties. In the latter reactions, the rate constant is the proportionality factor between the reaction velocity and the concentration of the starting products. Thus, it can be defined as the velocity for unit concentrations. The dimensions of k are sec.$^{-1}$ for first-order, and l. mol.$^{-1}$ sec.$^{-1}$ for second-order, reactions. The activation energy E is derived from the dependence on temperature of k according to Arrhenius's law.

In solid-state reactions, the concepts of concentration and order of reaction generally have no significance. The reaction velocity is defined here as the change with time of the thickness of the layer of product formed, or of the weight of this layer, or of the number of gram equivalents of product formed.

Consequently, a rate constant cannot be defined in the same way as for reactions in gases or solutions. If we accept the same conditions as for gas reactions, k must be independent of time and have the factor sec.$^{-1}$ in its dimensional formula, and increase with temperature according to an exponential law, from which an activation energy for the reaction could be derived. It will be difficult to predict whether the latter condition will be fulfilled, since the well-known assumption for gas reactions of an equilibrium between activated and non-activated molecules according to the Boltzmann distribution is not valid here. In certain cases, other circumstances will lead to the same exponential dependence on temperature of k.

This is generally the case for many reactions such as tarnishing reactions (for example, oxidations), substitution reactions and double decompositions which follow the parabolic reaction law. In these cases, the velocity is governed by a diffusion process through a growing layer. The velocity dx/dt is proportional to the reciprocal of x, the thickness of the layer; hence $dx/dt = k_1/x$, which leads to $x = (2k_1t)^{1/2}$. The rate constant k_1 is expressed in cm.^{2} sec.$^{-1}$.

If we consider the weight of the layer per unit area instead of its thickness, a rate constant k_2 having as dimensions gm.^{2} cm.$^{-4}$ sec.$^{-1}$ is defined. If we consider the number of gram equivalents of product formed, a new constant k_3 can be defined from the differential equation of reaction-rate with dimensions gm. equiv. cm.$^{-1}$ sec.$^{-1}$.

In tarnishing reactions, the rate-constant is generally proportional to the diffusion coefficient D of one of the reaction partners in the product formed. The exponential dependence on temperature of D leads to the validity of the Arrhenius relation for the rate constant:

$$k_1 = k_0 \exp(-E/RT)$$

where E is the activation energy for self-diffusion. Nevertheless, Jost[2] emphasizes that, on account of the complexity of the tarnishing process, a simple dependence on temperature of the net process often cannot be expected.

The theory of Wagner[3] for the velocity of substitution reactions and double decompositions, based on the model of the closed galvanic cell, leads to an expression for k which is proportional to the specific conductivity σ of the products formed. For the reaction $AgCl + Cu \rightarrow Ag + CuCl$, for example, k is proportional to σ_{CuCl}. The exponential dependence on temperature of k will be a consequence of the exponential dependence on temperature of σ in solids. The activation energy of the reaction will be that of electrical conduction (which is the same as for self-diffusion).

Thus, for reaction laws of the parabolic type, a rate constant can be defined in a similar way as for gas reactions, its exponential dependence on temperature included. Dimensionally it is dependent on the way the reaction velocity is defined.

Consider now a reaction following the linear law; for example, tarnishing reactions when the formed layer is porous or incoherent. Here, the reaction is governed by phase-boundary processes, and the velocity is independent on time:

$$dx/dt = k_4 \text{ or } x = k_4t$$

The constant k_4, which is expressed in cm. sec.$^{-1}$, is the rate of the phase-boundary process (for example, chemisorption) which will generally not increase exponentially with temperature. Consequently the Arrhenius relation will not be valid.

In solid state reactions governed by logarithmic laws, new difficulties arise on account of the presence of several constants independent of time and dependent on temperature.

Hence for solid state reaction kinetics, rate constant and activatoni energy can only be clearly defined when a suitable hypothesis for the mechanism of the given reaction is available. If the rate constant is defined from the experimental relation between the quantity of product formed and time, it is difficult to predict whether it will show an expon-

ential dependence on temperature. Even if this is approximately the case, the interpretation of the activation energy thus found remains dubious (see, for example, ref. 4).

Suppose that no hypothesis for the parabolic law was available, and that the rate constant k_s had been defined by $x = k_s t^{1/2}$. The activation energy deduced from the temperature dependence of k_s would not be E, the activation energy for diffusion, but $\frac{1}{2}E$:

$$k_s = (2k_1)^{1/2} = (2k_0)^{1/2}. \exp(-\tfrac{1}{2}E/RT)$$

Moreover, k_s has not the right dimensions (cm. sec.$^{-1/2}$ instead of cm.^{2} sec.$^{-1}$).

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Heat of Formation of the Difluoromethylene Radical

Atkinson[1] has accounted for the products of the mercury photosensitized decomposition of tetrafluoroethylene by supposing that the excited mercury atoms ($Hg\ ^3P_1$) are able to decompose tetrafluoroethylene to give two difluoromethylene radicals. This requires that the dissociation energy of the carbon–carbon bond in tetrafluoroethylene is equal to, or less than, 112 kcal./mole. Since this value is significantly smaller than the lower (125–30 kcal./mole)[2] of many values suggested for the dissociation energy of the carbon–carbon bond in ethylene, it is of some interest to obtain independent estimates of the heat of formation of the difluoromethylene radical.

The fluorobenzene ion ($C_6H_5F^+$) is an abundant species in the mass spectrum of benzotrifluoride. Similarly, difluorobenzene ions are abundant in the mass spectra of fluorobenzotrifluorides. This appears to be a specific rearrangement similar to that observed by Beynon[3] in the case of oxygen-containing compounds. Energy considerations suggest that the most probable process in these cases involves the expulsion of a difluoromethylene radical from the trifluoromethyl group, as for example:

$$C_6H_5CF_3 + e \rightarrow C_6H_5F^+ + CF_2 + 2e$$

In this case, the appearance potential ($A(C_6H_5F^+)$) of the fluorobenzene ion (13·35 eV.) taken together with the ionization potential ($I(C_6H_5F)$) of fluorobenzene (9·30 eV., cf. the value of 9·20 eV. from photoionization work[4]), and the heats of formation of fluorobenzene[5] (−26·5 kcal./mole) and of benzotrifluoride[6] (−138·9 kcal./mole), the heat of formation of the difluoromethylene radical is found to be equal to or less than −17 kcal./mole. Thus, using the value for the heat of formation of tetrafluoroethylene[7] (−152 kcal./mole), the dissociation energy of the carbon–carbon bond in this compound is found to be 118 kcal./mole. Within the uncertainties in the experimental quantities (which amount to about ± 5 kcal./mole) this is a maximum value for this quantity. In a similar way the appearance potential (13·15 eV.) of the *p*-difluorobenzene ion from *p*-fluorobenzotrifluoride together with the ionization potential of *p*-difluorobenzene (9·15 eV.), the heat of formation of *p*-difluorobenzene (−72·2 kcal./mole, calculated from $\Delta H_f(p\text{-}C_6H_4F_2)\ (l) = -79{\cdot}5$ (Scott, D. W., private communication), taking ΔH_v (estimated) = 7·3 kcal./mole), and the heat of formation of *p*-fluorobenzotrifluoride (assumed to be close to that of *m*-fluorobenzotrifluoride, −184·2 kcal./mole (Scott, D. W., private communication)), give a further estimate for the heat of formation of difluoromethylene (−21 kcal./mole) consistent with the first value. Since there is no value available for the ionization potential of *m*-difluorobenzene it is impossible to make any calculation based on the appearance potential (13·75 eV.) of the ion of this molecule from *m*-fluorobenzotrifluoride.

A less-certain but independent estimate of the heat of formation of the difluoromethylene radical may be obtained from some kinetic data of Atkinson and Atkinson[8], who have shown that octafluorocyclobutane is able to decompose by the process:

$$c\text{-}C_4F_8 \rightarrow CF_3\text{—}CF{=}CF_2 + CF_2$$

The energy of activation for this process must fulfil the condition:

$$E \geqslant \Delta H_f(CF_3CF{=}CF_2) + \Delta H_f(CF_2) - \Delta H_f(c\text{-}C_4F_8)$$

Atkinson and Atkinson[8] give for the rate coefficient for this reaction:

$$k = 3{\cdot}9 \times 10^{16} \exp -79{,}000/RT\ s^{-1}$$

Taking the energy of activation together with the heats of formation of octafluorocyclobutane (−352 kcal./mole from the heat of dimerization[10] and the heat of formation[6] of tetrafluoroethylene) and of hexafluoropropene (−259 from Duus's results[11], and the heat of formation of tetrafluoroethylene) requires that the heat of formation of difluoromethylene is equal to, or less than, −13 kcal./mole. The value quoted for the rate coefficient, however, was obtained from an analysis of the data that supposed that the quasi-stationary concentration of octafluorocyclobutane was controlled by its decomposition into two molecules of tetrafluoroethylene. A fuller analysis would probably require a slightly larger energy of activation and a larger pre-exponential factor for the rate coefficient, and this in turn would require a slightly more positive limiting value for the heat of formation of difluoromethylene.

Our value for the heat of formation of difluoromethylene (about −17 kcal./mole) supports the values proposed by Reed and Rabinowitch[12], and by Mann and Potocki[13]. It suggests that the radical is more stable than does the value (about −5 kcal./mole) implied by the results reported by Reed[14] from a study of electron impact processes with carbon tetrafluoride. Our conclusions about the bond dissociation energy in tetrafluoroethylene are similar to those of Margrave[15], but there remain the problems of the discrepancy between the value assumed by Margrave[15] for the ionization potential of the difluoromethylene radical (11 eV.) and that found by Reed[14] (13·35 eV.), and of the nature of the process by which the difluoromethylene ion is formed from tetrafluoroethylene. Our values for the heat of formation of difluoromethylene and the heat of formation of

the trifluoromethyl radical (−115 kcal./mole) give for the carbon–fluorine bond dissociation energy in the latter radical the value 117 kcal./mole. This is a little less than that (121 kcal./mole) of the carbon fluorine bond in carbon tetrafluoride[14].

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Dislocations as Active Centres in Heterogeneous Catalysis

Much work has been carried out in recent years on the relation of heterogeneous catalysis to point defects in solids or to semiconductivity. We have found an example of catalysis in which dislocations play the part of the active centre in the case of copper for the decomposition of diazonium salt (Gattermann's reaction). A sample of copper, free from point defects and containing dislocations only, is obtained by annealing the cold-worked sample in an appropriate temperature-range. The necessary data on annealing, a twisted sample, as given by Bons[1], are summarized in Fig. 1.

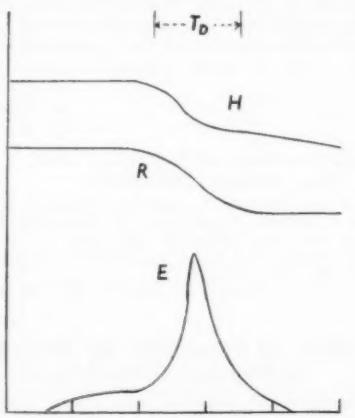

Fig. 1. Changes of hardness (H) and electrical resistivity (R), and the release of defect energy (E) during annealing of copper samples (99·96 per cent) deformed in torsion to $nd/l = 1·8$, where n is the number of turns, d the diameter and l the length (see ref. 1)

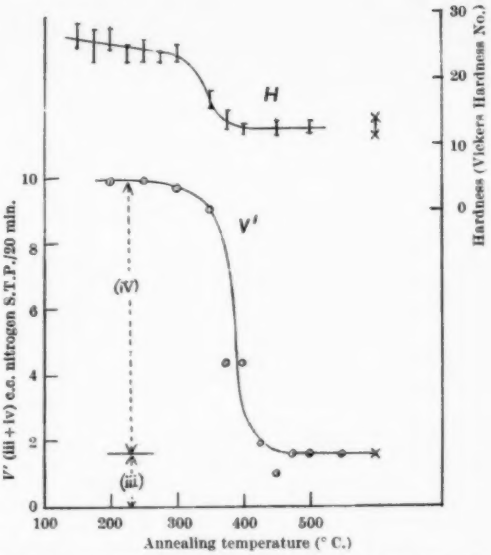

Fig. 2. The heterogeneous catalytic activity at 25° (V') and hardness (H) of copper cold-worked and annealed at various temperatures. ×, Values for samples not cold-worked

In a temperature-range T_D, a sudden change takes place in hardness, in electric resistivity and in density, with the rapid release of defect energy and recrystallization[2]. These phenomena have been attributed to the disappearance of dislocation in the deformed metal, because point defects produced in copper by deformation or irradiation at sub-zero temperatures disappear by annealing below room temperature.

In our experiments pieces of copper wire (99·96 per cent pure) were twisted to $nd/l = 1·0$ after complete annealing at 550°, and then were annealed again at various temperatures. The samples were washed with ammonia water and thrown into a solution of diazonium chloride; the reaction velocity was measured by the total volume of nitrogen (V) evolved in 20 min.; the part of V to be ascribed to heterogeneous catalysis (V') is shown in Fig. 2 together with hardness of the samples. Though the value of T_D is considerably influenced by impurities as well as by the degree of cold-working of different samples, the sudden and concurrent changes in hardness and in catalytic activity in the annealing temperature-range, 300–430° C., are ascribed to the disappearance of dislocations. Consequently, it may be concluded that the reaction corresponding to (iv) in Fig. 2 is a catalytic effect due to dislocations, amounting to 84 per cent of heterogeneous catalysis in the case shown. The value of V consists of the rate of (i) natural decomposition, (ii) homogeneous decomposition catalysed by cuprous ion dissolved from the metal, (iii) heterogeneous decomposition catalysed by the normal surface of copper and (iv) heterogeneous decomposition catalysed by the end of the dislocation at the surface. The change of surface area on annealing is considered to be negligible, because it was found that catalytically active copper powder deposited from copper sulphate solution by means of the reaction with zinc dust has almost the same adsorption capacity for methylene blue even after it is annealed at 500° and loses most of the activity

($3{\cdot}2 \times 10^{-7}$ and $3{\cdot}1 \times 10^{-7}$ mole/gm., respectively). The volume of nitrogen evolved, V, for a sample without dislocations (obtained by annealing at temperatures higher than T_D) is the sum of (i), (ii) and (iii), and the decrease in V on removing copper from the solution is the sum of (iii) and (iv) when reduced to the initial concentration of the solution, hence each value can be obtained separately. For example, (i) is 4·6, (ii) 1·5, (iii) 1·6 and (iv) 8·3 c.c. for samples annealed below T_D as shown in Fig. 2, (ii) as well as (iii) being almost constant irrespective of the annealing temperature.

In the case of nickel, the catalytic activity for the hydrogenation of ethylene is greatly enhanced by rolling the metal foil, but this effect is eliminated by annealing at a temperature between 200° and 300° (ref. 3). From the results of annealing experiments for deformed nickel[1,4], the evolution of energy and the change of physical properties between 90° and 320° and those between 520° and 660° were concluded to be due to the disappearance of vacancies and dislocations, respectively. Consequently, the greater proportion of the enhanced activity found by us may be attributed to point defects at the surface formed by cold-working (although the value of T_D may not be exactly the same as that with vacancies in the bulk crystal), contrary to Cratly and Granato's postulate[5] ascribing the activity to dislocations. By means of the method described, we hope to obtain some knowledge of the physical nature of the active centres in metallic catalysts.

We wish to thank Dr. M. Kikkawa and the late Mr. H. Ushio for supplying us with copper samples, and Prof. H. Wakeshima for his advice.

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BIOCHEMISTRY

Polysaccharide Content of the Prolapsed Nucleus Pulposus of the Human Intervertebral Disk

The nucleus pulposus of normal human intervertebral disk contains the two acidic mucopolysaccharides, chondroitin sulphate and keratosulphate[1–3]. During ageing an increase of collagen occurs[4] leading to a decreased ratio of mucopolysaccharide to collagen, although the absolute amount of mucopolysaccharide remains constant[4].

A recent paper by Hendry[5] has shown that the prolapsed nucleus pulposus is in fact relatively desiccated *in situ*. He postulated that this was due to a loss or deterioration of the protein–polysaccharide complexes present. We have analysed a series of nuclei pulposi, from prolapsed disks, for ester-sulphate and have found that without exception these contain very low amounts compared with our measured normal specimens.

The values obtained for the prolapsed nuclei pulposi are considerably lower (in most cases less than half) than values in the literature for the normal nucleus. The decrease in ester-sulphate content on ageing shown in Table 1 is apparent rather than absolute, due to increase of collagen increasing the total percentage dry weight. It is unlikely that all these low ester-sulphate values are only due to an abnormal increase in the collagen content of the nucleus; in fact, percentage dry weights of up to 75 per cent would be required to explain these values. It seems more likely that a genuine decrease in the absolute quantity of mucopolysaccharides has occurred before or during prolapse.

Table 1. Ester-Sulphate Analyses of Prolapsed Human Nuclei Pulposi at Various Ages

Age (yr.)	Ester-sulphate sulphur as percentage of dry weight
18 *f*	1·1
19 *f*	1·2
26 *m*	1·0
39 *m*	1·0
49 *m*	0·6
53 *f*	0·6

m, Male; *f*, female (free sulphate in all cases was found to be negligible).

It is seen that these results appear to favour Hendry's theory of relative dehydration of the nucleus leading to prolapse. An alternative hypothesis arises which involves the possibility that the normal deposition of collagen fibrils, which with age tends to make an intervertebral disk more rigid and less likely to prolapse, might not occur so completely with a genuine deficiency of mucopolysaccharide, thus allowing the nucleus pulposus to remain a relatively unstrengthened gel. Such a disk would then be the one more liable to prolapse than a normal disk of the same age group. The possibility arises that the mucopolysaccharides in the surrounding annulus fibrosus may also be reduced, giving rise to more friable wall structure.

The cause of the loss in acidic mucopolysaccharides is unknown, although it is of interest that we have found that all samples of nuclei pulposi contain a hitherto unreported free monosubstituted guanidine compound (Sakaguchi test and electrophoretic isolation).

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Metabolism of Propionate by Homogenates of Normal Sheep Liver

Propionic acid, one of the major products of cellulose fermentation in the ruminant stomach, is of unique importance in the carbohydrate economy of the sheep[1], in addition to its presumed function as a direct source of energy. Following injection of propionate into the blood-stream of a fasting sheep, there may be observed both a sharp rise in blood

glucose[2], and an increase in the rate of consumption of oxygen of the animal.

This communication deals with the metabolism of propionate by whole homogenates of sheep liver, prepared to retain mitochondrial respiration. Measurements were made of the rate of consumption of propionate and the rate of uptake of oxygen. In addition, the nature of the products of propionate metabolism was examined, and a hypothesis is proposed which relates these findings to the mechanism of propionate metabolism by the sheep.

The experimental conditions were designed to permit the measurement of oxygen consumption in an atmosphere of 95 per cent oxygen, 5 per cent carbon dioxide, by the indirect method in ref. 3. The apparent solubility of carbon dioxide in the medium used was determined to be 1·57 μl. carbon dioxide/μl. fluid/atmosphere (37° C.). Volumes of 6 ml. and 3 ml., containing 1·0 ml. and 0·5 ml. of a 1/7 homogenate in 0·25 *M* sucrose, were used, the high solubility of carbon dioxide in the medium permitting standard Warburg flasks to be used despite the similar gas volumes of the pairs of flasks. Replicate measurements indicate a precision of ±6 per cent for oxygen consumption-rates, and ±9 per cent for rates of evolution of carbon dioxide.

It was found that propionate was not consumed in the absence of oxygen, carbon dioxide, adenosine triphosphate (ATP) (or adenosine diphosphate), or of additional cytochrome *c*. In the complete medium the mean rate of propionate consumption was 2·39 μequiv. / mgm. nitrogen / hr., with a standard error of 0·15 (eighteen observations). Gas-liquid chromatography[4] of reaction products failed to demonstrate either the accumulation of other volatile acids, or the disappearance of any volatile acid other than propionic.

Fig. 1 shows the relationship between the rate of propionate consumption and the rate of uptake of oxygen, only those experiments having been included in which it was demonstrated that the rate of consumption of propionate was identical in both 6-ml. and 3-ml. volumes. This criterion is necessary because only under these conditions is the measure of oxygen consumption-rate valid, and because the rate of propionate consumption was found to be extremely sensitive to loss of carbon dioxide from the medium during the initial manipulations. The regression derived from the results shown in Fig. 1 yields a value of 39·1 ± *S.E.* 1·0 μl. oxygen/μequiv. of propionate consumed; this is equivalent to the complete oxidation of half the propionate metabolized.

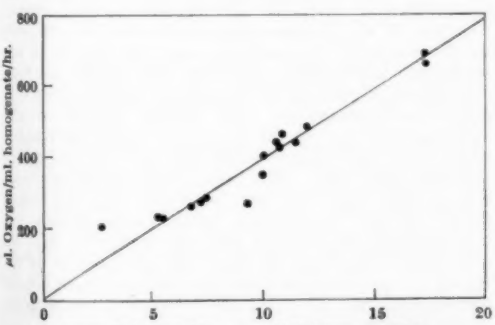

Fig. 1. Relation between uptake of oxygen and consumption of propionate

Experimental conditions were as described in the legend to Table 1, but with varying homogenate concentrations. Propionic acid consumption was measured as steam-volatile acid consumed, volatile acid being distilled from constant volume and titrated under nitrogen

The only detectable products of propionate metabolism were carbon dioxide and the dicarboxylic acids succinic acid, fumaric acid and malic acid. Lactic acid production, presumably from endogenous glycolysis, was identical in the presence and absence of propionate and no consistent effect was found on the small endogenous ketone production. The dicarboxylic acids were detected following exhaustive extraction with ether, by paper chromatography using four different solvent systems[5–8]. Methyl malonic acid could not be detected in these reaction mixtures, but has been found to accumulate when propionyl coenzyme A and labelled carbon dioxide are incubated with sheep liver homogenates in which mitochondrial structure has been disrupted by homogenizing in *p*H 8 *tris* buffer for 5 min. in a Servall Omni-mixer.

Table 1 shows the rates of uptake of oxygen by homogenates respiring in the presence of succinate, L-malate and propionate. These rates are consistent with an oxidation of propionate via L-malate, and since it has also been found that the stimulation in the rates of oxygen consumption caused by propionate and L-malate is not additive, it is inferred that propionate oxidation proceeds via the complete oxidation of L-malate.

Table 1. Oxidation of Propionate, Succinate and Malate by Sheep Liver Homogenates

Exp. No.	μl. oxygen/mgm. nitrogen/hr.			
	No substrate	propionate	succinate	malate
25	48	100	168	103
26	27	60	125	83
27	28	76	125	85
35	50	110	173	120

Oxygen consumption was measured by the indirect method of Warburg in 6·0 ml. and 3·0 ml. volumes of a medium having the following composition: KH_2PO_4 $3·6 \times 10^{-3}$ *M*, K_2HPO_4 $1·64 \times 10^{-3}$ *M*, $NaHCO_3$ $2·50 \times 10^{-2}$ *M*, KCl $9·0 \times 10^{-2}$ *M*, $MgCl_2$ 5×10^{-3} *M*, sucrose $4·0 \times 10^{-2}$ *M*, ATP $1·3 \times 10^{-3}$ *M*, cytochrome *c* $1·1 \times 10^{-4}$ *M*, substrate $5·0 \times 10^{-3}$ *M* and liver protein contributing 3–4 mgm. nitrogen/6·0 ml. After gassing with 95 per cent oxygen, 5 per cent carbon dioxide for 9 min. in the bath at 37° C., flasks were equilibrated for 10 min. and buffered isotonic substrate added from the side-arm to a final concentration of $5·0 \times 10^{-3}$ *M*. Manometric readings were taken at 6-min. intervals for 36 min., oxygen consumption-rates being computed over the final 30 min. Homogenates were prepared from the livers of freshly killed sheep in 0·25 *M* sucrose in a glass homogenizer immersed in ice water. Nuclei and cell debris were removed by centrifuging at 600*g* for 10 min. in a refrigerated centrifuge.

In attempting to explain the quantitative link between the rates of consumption of propionate and uptake of oxygen, two possibilities have been considered, either of which may be expressed by the reaction sequence shown in Fig. 2, in which it is proposed that the complete oxidation of 1 mole of L-malate leads to the activation of 2 moles of carbon dioxide.

One means by which this could be achieved is by the maintenance of a stable rate of oxidative phosphorylation. Assuming the activation of propionate to release pyrophosphate[9], and the fixation of carbon dioxide to release orthophosphate[10], then the P/O ratio necessary to sustain the rate of propionate uptake found would be 6/7 (0·86 ± 0·02; cf. Fig. 1), a curious value, maintained with unusual precision.

A more probable explanation may lie in the direct transfer to propionyl coenzyme A of carbon dioxide derived from oxidation of the malate carbon skeleton.

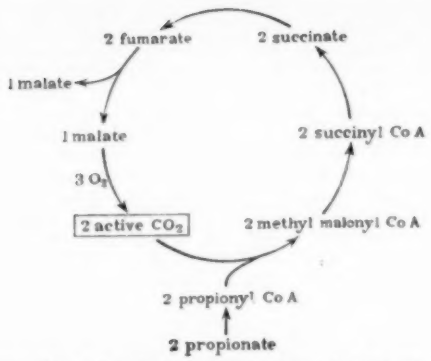

Fig. 2. Proposed mechanism of propionate metabolism by sheep liver

The recent observation of Swick and Wood[11] of the direct transfer of the oxalacetate β carboxyl group to propionyl coenzyme A to form methyl malonyl coenzyme A in cell-free extracts of *Propionibacterium shermanii* supports this hypothesis. Swick and Wood pointed out that such transferable carboxyl groups exist in methyl malonyl coenzyme A and malonyl coenzyme A in addition to oxalacetic acid, and that these molecules have a common structural feature in that the active carbon dioxide group is derived from a carboxyl group β to a carbonyl function which is in turn adjacent either to a second carboxyl group or to a coenzyme A moiety. During complete oxidation of malate via pyruvate and the tricarboxylic acid cycle, both oxalacetic acid and oxalosuccinic acid lose carboxyl groups of this nature. With this in mind, work on the mechanism of propionyl coenzyme A carboxylation in sheep liver mitochondria is being continued.

The relationship between uptake of oxygen and consumption of propionate by liver homogenates is of considerable interest in relation to the *in vivo* synthesis of glucose from propionate. The observations reported here demonstrate a mechanism whereby precursors of carbohydrate are derived from propionate at twice the rate at which propionate may be oxidized.

We thank Dr. H. R. Marston for suggesting this work, which was undertaken as part of a general investigation of cobalt deficiency in sheep.

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Binding of *RP2-L*—a Nuclear Protein of Neoplastic Tissues—to Deoxyribonucleic Acid

Recent work in this laboratory has indicated that the incorporation of radioactive amino-acids into nuclear proteins, especially the acid-soluble nuclear proteins, represents an important metabolic pathway in transplantable rat tumours[1–3]. The acid-soluble nuclear proteins obtained from rats injected with L-lysine-U-^{14}C were chromatographed on carboxymethyl-cellulose columns[4] after the acid extracts had been dialysed against 0·5 *N* acetic acid. The cellulose columns (sodium form) had been equilibrated against 0·05 *M* sodium acetate buffer, *p*H 4·0. Gradient elution was used with *N* formic acid followed by 8 *N* formic acid. All procedures were carried out at 4° C. The resolving power of this method provided specific chromatographic patterns for protein distribution and distribution of radioactivity for the acid-soluble nuclear proteins of the Walker tumour and various tissues of the tumour-bearing rat. The chromatograms of the acid-soluble nuclear proteins from the various non-tumour tissues contained one to three radioactive peaks with relatively low specific activities. The chromatograms of the nuclear extracts of the Walker tumour, and a number of other malignant tumours, contained a radioactive peak which was not found in any of the growing or non-growing[4,5] non-tumour tissues studied.

In the present work, deoxyribonucleoproteins were extracted with water from cell nuclei, isolated from the Walker tumour and liver of tumour-bearing rats[6–10]. The deoxyribonucleoproteins were then precipitated by making the medium 0·15 *M* with respect to sodium chloride (ref. 10). L-lysine-U-^{14}C (10 μc.) was injected 1 hr. before the tissues were excised[3,4]. The nuclei from 3–5 gm. of tissue were blended in 50 ml. distilled water 6 times for periods of 10 sec. The temperature was maintained at 4° C. The sample was centrifuged at 2,000*g* for 30 min. and the nuclear residue was washed twice with 50 ml. distilled water. To the combined supernatant solutions containing the deoxyribonucleoproteins, solid sodium chloride was added to make a final concentration of 0·15 *M* and the sample was kept in the cold laboratory (4° C. for 1 hr.) and was again centrifuged at 2,000*g* for 30 min. after the supernatant solution (the 'nuclear sap') was decanted. The white deoxyribonucleoprotein precipitate was stirred with 0·25 *N* hydrochloric acid for 20 min. and then was centrifuged at 100,000*g* for 30 min. After centrifugation of the supernatant nuclear sap at 100,000*g* for 30 min., 2 *N* hydrochloric acid was added to the combined supernatant solutions to make a final concentration of 0·25 *N* hydrochloric acid. Of the total deoxyribonucleic acid (DNA) found in the various fractions, 80–90 per cent was in the residue which was precipitated after the acid extraction of the nucleoproteins. The remaining 10–20 per cent was in the water-insoluble residue. No DNA was found in the supernatant solutions in which the concentration of sodium chloride was 0·15 *M*. In this communication the DNA-bound protein is referred to as 'chromosomal protein' and proteins of the supernatant fractions are referred to as proteins of the nuclear sap.

The optical densities at 280 mμ of a standard volume of 3·0 ml. of extracts of chromosomal proteins of tumour and liver respectively were 0·30 and 0·20 per gm. wet weight of tissue. The optical densities of the acid-soluble proteins of the nuclear sap of tumour and liver respectively were 2·0 and 1·0. The

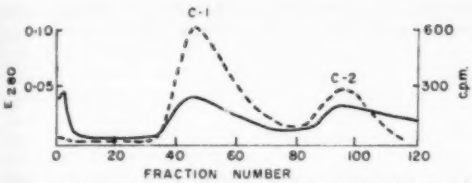

Fig. 1. Chromatographic patterns of both radioactivity and protein-concentration for chromosomal proteins of the Walker 256 carcinosarcoma. The data are averages of three experiments. Gradient elution was employed with *N* formic acid followed by elution with 8 *N* formic acid at fraction 80. Solid line, optical density; broken line, radioactivity

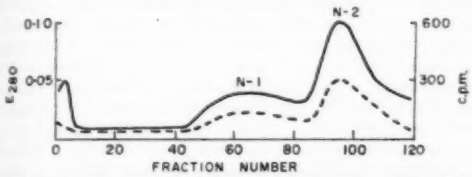

Fig. 2. Chromatographic patterns of both radioactivity and protein-concentration for nuclear sap proteins of the Walker 256 carcinosarcoma. The data are averages of three experiments. Solid line, optical density; broken line, radioactivity

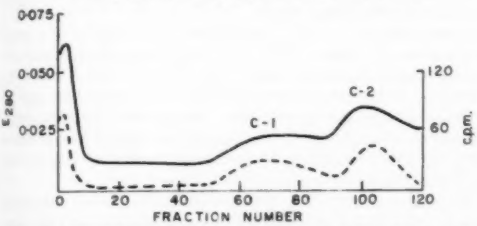

Fig. 3. Chromatographic patterns of both radioactivity and protein-concentration for chromosomal proteins of the liver of the tumour-bearing rat. The data are averages of three experiments. Solid line, optical density; broken line, radioactivity

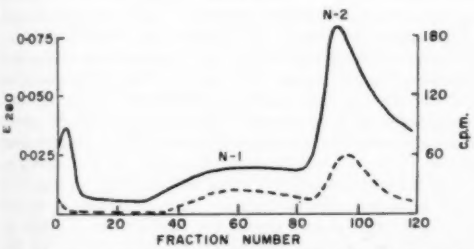

Fig. 4. Chromatographic patterns of both radioactivity and protein-concentration for nuclear sap proteins of the liver of the tumour-bearing rat. The data are averages of two experiments. Solid line, optical density; broken line, radioactivity

extracts obtained were chromatographed on carboxymethylcellulose as described above, after dialysis against 0·5 *N* acetic acid.

In order to maintain maximum resolution of the proteins, extracts of 'chromosomal proteins' from 4–6 gm. of tissue and extracts of nuclear sap from 2–3 gm. of tissue were chromatographed.

The patterns for the protein distribution and radioactivity in the chromatograms of 'chromosomal' (DNA-bound) proteins and the cationic proteins of the nuclear sap of tumour and liver are presented in Figs. 1–4. The specific activity of the chromosomal proteins of the tumour was much higher than that of the other extracts. The most radioactive proteins, that is *C*–1 of the tumour (Fig. 1), were eluted with *N* formic acid in the same position as *RP2–L*, the protein peak found in neoplastic tissues. Like *RP2–L*, the specific activity of the protein of peak *C*–1 was high (10,050 c.p.m./E_{280}). In addition, the protein of peak *C*–1 of the tumour contained 35 per cent of the total counts of the total acid extract. Since *C*–1 or *RP2–L* was concomitantly dissolved and precipitated with DNA, and was not found in the preparations which did not contain DNA, these data indicate that *C*–1 or *RP2–L* is a DNA-bound chromosomal protein.

The finding that a protein, found thus far only in neoplastic tissues, is synthesized rapidly on the chromosomes suggests that the genetic change in tumour cells may be reflected in production of abnormal chromatin. These findings may provide a tool for investigation of the nature of the abnormalities of the DNA in neoplastic cells.

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Isolation and Identification of Rhamnose from Rabbit Skin

The presence of neutral sugars such as galactose, mannose and L-fucose in several animal sources such as glycoproteins or blood group substances is well known[1] but L-rhamnose has not been previously reported as a constituent of mammalian tissues.

Skin from rabbits (1–2 years old), injected with glucose-U-^{14}C, was treated with a depilatory, cut into strips, frozen in liquid nitrogen and ground into a fine powder in a Wiley mill. The powder was homogenized with water in a Virtis-45 homogenizer at maximum speed for 30 min., the extract centrifuged at 5,000 r.p.m. for 30 min., the supernatant filtered through glass wool and lyophilized to yield 0·10–0·20 gm./10 gm. of milled powder.

Hydrolysis of the lyophilized material with 0·25 *N* hydrochloric acid for 30 min.–1 hr., followed by methyl pentose analysis[2] of the supernatant, indicated that the lyophilized material contained 1–3 mgm. methyl pentose/100 mgm. of material. The presence of rhamnose was suggested by the relative mobility of reducing substances in butanol/pyridine/water (6 : 4 : 3), butanol/acetic acid/water (4 : 1 : 5) and isopropanol/water (9 : 1)[3–5]. The latter solvent gave the best separations from other methyl pentoses such as fucose.

250 mgm. of the water-soluble fraction were hydrolysed as above (1 hr.) and salts removed on a 'Dowex 50 H^+–Dowex 1', HCO_3^- mixed-bed resin.

The resulting solution was concentrated, banded on acetic acid washed Whatman *BMM* paper, and chromatographed for 17–20 hr. at room temperature

in a solvent system of 9 parts isopropanol : 1 part water. Visualization of reducing substances with silver nitrate on a parallel strip showed three spots, one of which had a mobility corresponding to that of rhamnose. The appropriate area was eluted with water, and an aliquot assayed for radioactivity in a Packard 'Tri-Carb' liquid scintillation counter using dioxane/amisole/dimethoxyethane (6 : 1 : 1) as solvent and 2,5-diphenyl oxazole 1,4-*bis*-2-(5-phenyloxazolyl) benzene (40 : 1). This fraction was found to contain carbon-14. 50·0 mgm. of crystalline L-rhamnose hydrate was added as carrier, the solution concentrated to a thick syrup and allowed to crystallize for 2 hr.–3 days. The crystalline rhamnose obtained in several experiments was identified by infra-red spectrometry and contained 85–98 per cent of the total radioactivity present in the water eluate of the chromatogram; the specific activity was not lowered on recrystallization.

The fine structure of the rhamnose-containing compound is at present unknown and will be the subject of subsequent investigation.

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Formation of Histamine and Histamine-like Substances from Histidine by Quartz Dust

It has been shown[1] that quartz dust is capable of participating in a number of oxidative and hydroxylative reactions. The present communication reports the production of histamine, from the interaction of quartz dust with histidine, and the chromatographic isolation of additional products of this reaction, namely, imidazole-carboxylic acids from the lungs of guinea pigs treated with quartz dust.

Attention was first directed to a possibly harmful effect of histamine in silicosis by Uspensky *et al.*[2], who in 1957 reported an overall increase of this material in the lungs of silicotic animals over that in the lungs of normal animals, and ascribed the toxic action of quartz to its release of histamine in excessive amounts into the tissue.

It has now been shown in this laboratory that quartz dust, when treated with the amino-acid *dl*-histidine base, produces several imidazole-like substances, one of which has been identified as histamine both chromatographically (descending unidimensional system using Whatman No. 1 paper, *n*-propanol / 0·2 *N* ammonia (3 : 1); spraying reagent: Pauly's sulphanilic acid reagent) and biologically (guinea pig uterus). Similar chromatographic products were obtained when hydrogen peroxide was treated with histidine under the same conditions. The reaction of quartz with histidine may be of the oxidation-reduction type due to the peroxidative properties of quartz reported earlier[1]. Deamination and partial decarboxylation of histidine were obtained by Holtz[3] by treating it with ascorbic acid and glutathione in air or oxygen, or by passing oxygen and hydrogen through a medium containing histidine and metal catalysts.

In the present work a yield of at least 5 μgm. histamine (0·1 per cent) was obtained by alternatively shaking and incubating 1 gm. of quartz dust with 5 mgm. histidine in 5 ml. water at 37° for 5–10 days. After centrifugation, the dust was washed with ethanol–hydrochloric acid and this washing was added to the supernatant mother liquor before concentrating to about 0·2–0·5 ml. The reaction was accelerated and the yield was increased when the medium was made slightly alkaline with sodium carbonate. This was also found when the contents of the vessel were allowed to dry out during shaking. When carried out in acid solution (hydrochloric acid), which also stabilized any histamine formed, the reaction took place rapidly at 85–90° C. Iron ions in the medium either retarded or inhibited histamine formation: this finding agrees with that of Holtz[3]. Furthermore, acid-washed quartz produced more histamine from histidine than did untreated quartz with an iron content of 0·03 mgm./gm.

The asbestos dusts, crocidolite and chrysotile, and mine dust (a dust collected from ventilation shafts in a Witwatersrand gold mine) were also able to produce histamine from histidine in the presence of sodium carbonate, but the relatively inert dusts, kaolin and talc, were without effect. These latter have already been reported[1] to have low or negligible oxidizing or hydroxylating abilities.

Dusts producing histamine also gave rise to a second Pauly-positive material which was detected chromatographically (orange red, R_F value 0·1–0·14), and which was later identified by the use of other solvents as a complex spot consisting of a number of imidazole carboxylic acids. Glutamic acid, a well-known degradation product of histidine[4], was also produced.

Quantitative assays of lung tissue for histamine indicated that this reaction between active dusts and histidine might occur *in vivo*. The assays were carried out on the wet, unperfused lungs of two groups of four guinea pigs; the animals of one group were exposed for 140 days to a superfine quartz dust (80 per cent of particles less than 2μ) at a concentration of 25,000 particles/c.c. for about 7½ hr. a day; the other group were controls. A mean value of 8·7 mgm./100 gm. dried tissue for histamine (as the dihydrochloride) was obtained for the lungs of the group treated with quartz dust compared with 5·4 mgm./100 gm. for the control group. This represents a 29 per cent increase of histamine in the dusted groups of animals. In a further group of animals dusted for a period of 180 days, the increase was of the same order (namely, 31 per cent). Chromatographic analyses of the trichloroacetic acid extracts of lungs after adsorption with activated charcoal and elution with ethanol / hydrochloric acid (2 : 1) showed the presence in the dusted group of the Pauly-positive spot described above (R_F 0·1–0·14), but not in the control sample even when much higher concentrations of lung extracts were used. This spot, however, was absent when lung extracts of animals treated with dust for only 70 days were chromatographed. On further resolution in other chromatographic solvent systems, the imidazole carboxylic acids listed in Table 1 were identified. In addition, traces of urocanic acid were identified in lung extracts from

Table 1. R_F VALUES OF MATERIALS FOUND IN TWO SOLVENT SYSTEMS

Solvent system	Material	R_F value
n-Butanol/acetic acid/ water (50 : 12 : 50)	Imidazole pyruvic acid	0·24
	Imidazole lactic acid	0·27
	Imidazole acetic acid	0·34
	Hydroxymethyl imidazole	0·41
Isopropanol/ammonia (0·88)/ water (160 : 8 : 16)	Imidazole pyruvic acid	0·04
	Imidazole lactic acid	0·07
	Imidazole acetic acid	0·06

animals treated with dust; this might be a hydrolysis product of its choline ester, murexine, a substance producing pronounced pharmacological effects. Very small amounts, or none, of these materials were detected in extracts from the lungs of the control group. The enzymatic conversion of histidine to some of these degradation products has been reported by van Thoai[5], who treated L-amino-acid-oxidase with histidine.

The evidence obtained from these experiments suggests that not only can quartz produce histamine from histidine *in vitro*, but also a number of other derivatives, some of which are biologically active. The presence of these substances in the lungs of animals exposed to quartz dust but not in controls makes it seem likely that the *in vitro* course of events shown above may occur *in vivo*.

The possibility of histidine as a basic substance being adsorbed on quartz dust after this has entered the lung tissue, and its continual transformation into small amounts of histamine and other potentially harmful substances might over a long period of time be of importance in the pathogenesis of silicosis.

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Influence of *p*H and Urea on the Ultra-violet Fluorescence of Several Globular Proteins

RECENT work by Weber[1–3] has shown that the ultra-violet fluorescent spectra of globular proteins differ from those predicted for the summation of the independent contributions of their aromatic amino-acid constituents. Those examples investigated which contained tyrosine, but no tryptophan, showed a tyrosine emission spectrum, but with a reduced quantum yield. Those containing both tyrosine and tryptophan showed an emission spectrum predominantly resembling that of tryptophan alone, with an emission maximum in the range 320–350 mμ. The present communication will be concerned solely with proteins of the second category.

These include a protein showing a reversible structural transition at extremes of *p*H (bovine serum albumin), a protein the internal structure of which is probably invariant to *p*H (lysozyme), and a protein undergoing a simultaneous denaturation and unfolding into a random coil at neutral *p*H (pepsin). An Aminco-Bowman spectrofluorometer, equipped with a thermostatted cell-holder, was used for all measurements. Unless otherwise specified, the temperature of measurement was 24° C. The wave-lengths of excitation and of emission were 290 mμ and 340 mμ, respectively.

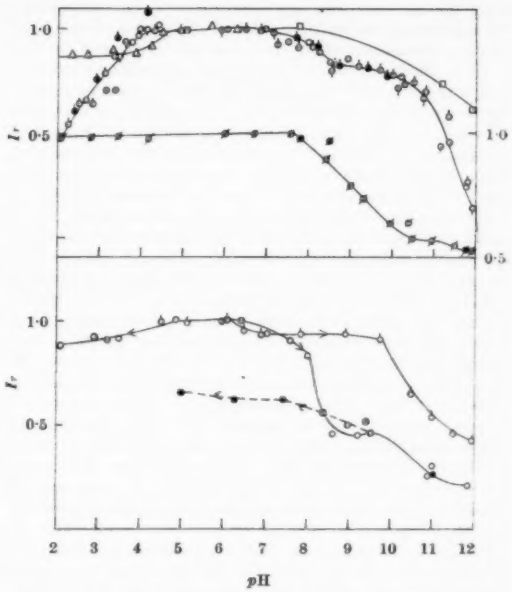

Fig. 1. Relative fluorescence intensities. Upper: ⚲, Armour bovine plasma albumin in water; ○, bovine plasma albumin fraction from diethylaminoethyl cellulose column (containing 0·24 mole —SH per mole albumin in water; △, same, in 2·0 *M* potassium chloride; □, same, in 8 *M* urea; ◎, bovine plasma albumin fraction from diethylaminoethyl cellulose column (containing 0·98 mole —SH per mole albumin) in water; ⊖, Armour crystalline lysozyme in water. The curve is displaced downward by 0·5 unit with respect to the albumin curve. The right-hand ordinate applies. Lower: ○, Armour crystalline pepsin in water; ◎, same, in 0·2 *M* potassium chloride. The protein concentration is 0·1 gm./l. in each case. The filled circles represent reverse points. The ordinate is the fluorescence intensity relative to that at *p*H 6, which is the starting point for either acid or alkaline titration. The wave-lengths of activation and of emission are 290 mμ and 340 mμ, respectively

All the proteins under examination had an emission spectrum characteristic of tryptophan, with a maximum in the range 320–350 mμ. The dependence of fluorescence intensity on *p*H was very different for the various proteins. All these had, however, the common feature of undergoing a pronounced quenching in the *p*H region 9–12 (Fig. 1).

In the cases of bovine serum albumin and lysozyme, the reverse curve obtained on back titration from alkaline *p*H showed no major deviation from the forward curve, in harmony with expectations arising from the reversible character of the alkaline titrations for these proteins.

The presence of urea in high concentration (10 *M*) appears to reduce the magnitude of alkaline quenching at a given *p*H for bovine serum albumin considerably.

At *p*H's acid to *p*H 5 the various proteins examined showed a wide divergence of behaviour. Lysozyme

and native pepsin, the macromolecular properties of which appear to be invariant to *p*H in this range, show a small decrease in intensity. However, bovine serum albumin, which is known to undergo a structural transition in this zone[6] of *p*H, shows a reversible quenching of fluorescence if the titration is carried out in the absence of added electrolyte. In 2·0 *M* potassium chloride the acid quenching is reduced somewhat, presumably because of the suppression under these conditions of the inflation of the molecular domain occurring at low ionic strengths[6].

In addition to the acid and alkaline quenchings bovine serum albumin showed a small but definite quenching in the region *p*H 7·0–9·0 (Fig. 1). It is of interest that spectral evidence exists for a minor structural change in this zone[7]. Katz and Klotz have reported changes in calcium ion binding properties in this region[8].

Pepsin, which is known to undergo an irreversible denaturation, accompanied by a gross molecular disorganization at a critical neutral *p*H zone[6–9], shows somewhat different behaviour[9]. The emission increases slightly between *p*H 2 and *p*H 5. The onset of irreversible denaturation, which occurs at *p*H 7·5–8·5 in the absence of added electrolyte, is reflected by a sharp drop in fluorescence intensity (Fig. 1). If 0·2 *M* potassium chloride is present the extent of the drop is greatly reduced. In either case a second region of decrease is noted in the zone of tyrosine ionization, *p*H 9–12.

A complete interpretation of this fairly complex behaviour will certainly require the disentangling of several effects in each of the examples considered. It is likely that the ionized form of tyrosine is the only group the absorption spectrum of which overlaps sufficiently with the tryptophan emission spectrum to permit an important degree of radiationless energy transfer[4,5]. From the behaviour of pepsin and bovine serum albumin, it is clear that the intensity of fluorescence of globular proteins is a function of their molecular organization and can be expected to be influenced by molecular events which alter the secondary or tertiary structure and thereby modify the environment of the fluorescent group.

Bovine plasma albumin fractions were obtained through the courtesy of Dr. R. Hartley.

Note added in proof. In subsequent work with another lysozyme preparation a minor (10 per cent) quenching was found between *p*H 6 and *p*H 2. The acid branch of the lysozyme curve of Fig. 1 may thus require revision.

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Retinene-1 in Insect Tissues

Attempts to detect vitamin A in insect tissues have been largely unsuccessful. One species of cockroach (*Blatella germanica*) has been raised for generations on a diet devoid of vitamin A and carotenoids[1]. As no vitamin A could be detected in oil extracted from these insects, it appeared that the vitamin played no part in their metabolic processes. Other workers[2] similarly have reported their inability to detect vitamin A in Blattidae. Acetone extracts of the locusts *Schistocerca gregaria* and *Locusta migratoria migratorioides* gave negative tests for the vitamin[3], while extracts of the heads of fruit-flies, grasshoppers, and dragonflies also have been reported to be lacking in vitamin A (ref. 4). No dietary requirement for vitamin A could be demonstrated for either *Drosophila melanogaster*[5,6] or *Anopheles labranchiae atroparvus*[7].

However, extracts of the pupæ of the silkworms *Bombyx mori* and *Antherea pernyi* have been reported[8,9] to contain vitamin A, while Goldsmith[10] recently has demonstrated that extracts of the heads of honey-bees contain retinene-1, and that a visual pigment of this insect is a rhodopsin compound analogous to vertebrate visual pigments. Wolken *et al.*, in a recent report[11], have announced the detection of retinene-1 in house-flies.

In the experiments reported here, the presence of retinene-1 in the honey-bee and the house-fly was confirmed, and the compound detected in extracts of the following insects, which represent many major orders of insects: *Paracolletes fulvescens* (Hymenoptera), *Locusta migratoria* (Orthoptera), *Uropetala carovei* (Odonata), *Cicindela tuberculata* (Coleoptera), *Nyctemera annulata* (Lepidoptera), *Cutelia sedilotti* (Orthoptera).

Adult specimens of these insects were collected locally, and in some cases were preserved by deep freezing, and in others were killed by decapitation and immediately experimented on. The heads were separated from the rest of the body and the two tissues extracted separately. In the case of the bees, the legs were removed to avoid excess carotenoids from pollen. The tissues were ground with anhydrous sodium sulphate and the mixture extracted with anhydrous acetone. This treatment releases carotenoids, vitamin A and retinenes from proteins. The resulting extracts were evaporated and the residues taken up in petroleum ether. On chromatography on aluminium oxide columns, yellow absorption bands developed, and were eluted with acetone–petroleum ether mixtures (4 per cent, 10 per cent and 40 per cent v/v). Each fraction was evaporated and the residues taken up in a small amount of chloroform. A Carr–Price reaction with saturated antimony trichloride solution in chloroform, and acetic anhydride, was conducted on each fraction. One fraction from insect heads of each species gave a noticeable blue coloration and an absorption maximum at 664 mμ.

These observations demonstrate the presence of retinene-1 in the heads, and its absence in the bodies, of each of the insect species investigated. It is a reasonable conclusion, considering the known functions of retinene in vertebrates and in other invertebrate phyla, that the retinene detected occurs in the insect eyes and is involved in their visual processes. It is of considerable interest that no vitamin A alcohol was detected in the above experiments. Moreover, the amounts of retinene present in the insect heads was very small and about 10 gm.

of tissue was necessary to give a satisfactory positive result.

These findings indicate that the rhodopsin type of visual pigment occurs in many insects. This being the case, the experiments[1,5–7] in which insects have been raised on diets devoid of vitamin A and carotenoids are difficult to understand. Perhaps there is some other insect visual system that does not involve retinene, or alternatively, and more likely, perhaps the insects raised in these nutritional experiments were visually defective.

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PHYSIOLOGY

Oscillatory Flow in an Air-filled Elastic System

A REPORT has been published by me[1] of the study of oscillatory flow in a fluid-filled elastic system, using an 'oscillator'. It has now been discovered that the same device (Fig. 1) will oscillate, in stationary wave motion, when there passes through it a stream of air, instead of water or blood.

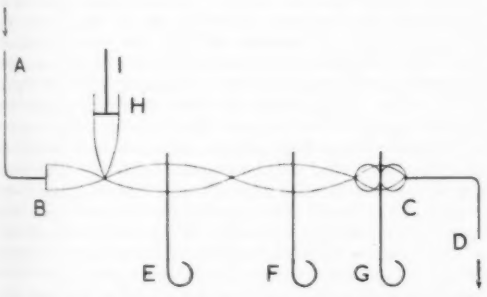

Fig. 1. Diagram to show the component parts of the 'oscillator'

Air compressed to a pressure of about 0·7 kgm./cm.^{2} is delivered from a tank of which the outlet is controlled by a screw valve. The air is led by the rigid tube (*A*) to the elastic tube (*BC*), which is composed of latex rubber, 0·7 cm. in diameter and 97 cm. long. The other end of *BC* is connected to the rigid outlet tube (*D*). Extensions of the torsion springs (*E*) and (*F*) compress the elastic tube at the sites of antinodes, the extension of the torsion spring (*G*), at the site of a pseudo-stationary node, the loops being as shown. The waves are both transverse and longitudinal, belonging to two systems of differing length, namely, 1–2 cm. and approximately 75 cm. As the wavelength approaches the diameter of the tube, the particles of air describe more or less circular orbits. The correct position of the springs may be determined previously, by running water through the model from a reservoir, as already described. At this stage, the quarter-wave matching stub (*H*) is useful in suppressing stationary waves at the proximal end of *BC*: one end of the stub is connected to a node, as shown, the other closed by the piston (*I*).

Using compressed air, the model can be made to produce a great variety of noises and sounds, including musical notes. Oscillations of low frequencies resemble purring noises: at high frequencies, squealing noises result. Harsh sounds occur, resembling those made by parrots or chirruping sounds such as those of other birds.

Tuning is effected by altering the pressure of the springs on the elastic tube. In the case of the spring (*G*), however, tuning is also effected by moving the point of application with relation to the junction of *BC* and *D*. Tuning is particularly sensitive at this site. The effect of transverse compression appears to be analogous to the application of a 'shunted inductance': the greater the pressure, the higher the frequency and conversely. Movement of the point of the spring, in relation to the end of the tube, alters the length of the system of short stationary waves. The segment of elastic tube involved can be regarded as a cavity resonator, so that the effect is analogous to that of altering the 'capacitance'. The shorter the wave-length, the higher the frequency and conversely. Increase of 'resistance', brought about by closing the screw valve which controls delivery of air, causes the pitch of the note, or noise, to rise and conversely.

The spring (*G*), pressing on the elastic tube, produces a shape closely resembling that of one vocal cord. It may be assumed that, in the larynx, the wave-lengths of the vibrating expired air approach the dimensions of this structure and of the related cavities. The system of long waves of the tube (*BC*) is then related to the vibrating columns of air in the trachea and bronchi during speech and the apparatus can be regarded as an analogue for study of the mechanism of phonation.

The model suggests that, in addition to approximation of the vocal cords, elevation and depression of the larynx when the pitch of the voice rises and falls, respectively, are also of significance in tuning. In phonation, moreover, the action of the thorax and lungs is that of velocity modulation of the expelled air, whereas that of the larynx is to effect density modulation of this air.

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Hormonal Control of the Development of the Thymus of the Fœtal Rabbit

THAT the fœtal adrenal is physiologically active has been firmly established; for example, Jost and Jacquot have shown its importance in the development of fœtal liver glycogen[1–3]. That the adrenal itself is influenced in its development by a structure or structures within the skull—generally assumed

to be the hypophysis—has been demonstrated in the rabbit[4,5] and rat[6,7] by fœtal decapitation, following which there is a considerable reduction in the adrenal by full term. Since it is well recognized that in the adult animal adrenal hormones have a thymolytic action, it was considered possible that the development of the fœtal thymus might be influenced by the fœtal adrenals. To test this hypothesis rabbit fœtuses were decapitated at 20–21 days of development and the thymus glands were weighed when the fœtuses had reached almost to term. The results were clear cut, for in the operated fœtuses the thymus on average was 72 per cent heavier than in their litter mate controls[5].

The operation of decapitation of the fœtus, performed to remove the pituitary, does not affect the development of the fœtus, as judged by gross weight[8,9]. The operated fœtuses, together with their litter mates, continue to develop within the uterine cavity for a further eight days. It was thought that the resulting increase in thymus weight might be the result of the reduction in the development of the adrenals secondary to the decapitation of the fœtus which abolishes fœtal pituitary secretions, in particular, fœtal adrenocorticotrophic hormone (ACTH)[5].

However, it could be argued that the increase in size of thymus in the decapitated fœtuses might be due to the absence of other fœtal pituitary hormones apart from ACTH, or even to the removal of some other structure in the head, such as the brain or the pineal. To investigate this point further, it was decided to inject ACTH into the fœtus, at the same time as the decapitation was performed, to replace the fœtal ACTH, and to investigate the effect of this combined procedure on the development of the adrenals and the thymus. A long-acting preparation of ACTH in gelatin was used to avoid having to repeat the injection into the fœtus.

Eight fœtuses were decapitated by the method described by Jost[10] between the 21st and 22nd day of development, and 0·2 ml. of 'Acthar' gel was injected subcutaneously in the interscapular region of each fœtus just before it was returned to the uterus. The fœtuses were recovered after a further seven days of intra-uterine development, by Cæsarian section, and the adrenals and thymus removed and weighed to the nearest 0·1 mgm. The weights were expressed per 100 gm. of body-weight, and were compared with 15 litter-mate controls.

The results are shown in Table 1. There is no significant difference between the weights of the decapitated fœtuses injected with ACTH and the litter-mate controls. The adrenals were found to be slightly larger in the decapitated fœtuses injected with ACTH compared with the control fœtuses, but this difference is not significant. The thymus of the experimental fœtuses showed no significant increase in weight over the thymus of the controls.

These results provide confirmation of the view that the increase in weight of thymus found in decapitated fœtuses[5] is due to the retarded adrenal development, caused by the absence of fœtal ACTH following the decapitation.

These findings also provide an explanation for some of the endocrine abnormalities present in the human anencephalic fœtus. It has long been known that the pituitary of these fœtuses is very small or absent[11], and the small adrenals and large thymus reported in this human abnormality[12] are likely to be secondary to the deficiency of fœtal ACTH.

I am indebted to Prof. A. Jost for his help with the technique involved in intra-uterine surgery of the fœtus, to the Medical Research Council for a grant for apparatus, to Armour Laboratories for a supply of ACTH, and to Prof. E. W. Walls for his help and encouragement in this work.

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Table 1. Thymus and Adrenal Weights of the Rabbit Fœtus following Decapitation and Injection of ACTH

Fœtuses	No.	Age at investigation (days)	Body-weight (gm.) headless	Adrenal weights (mgm./100 gm.)	Thymus weight (mgm./100 gm.)
Decapitated + ACTH (at 21–22 days)	8	28–29	23·4 ± 1·8	25·4 ± 4*	275·3 ± 13*
Controls	15	28–29	23·0 ± 1·5	19·6 ± 1*	261·6 ± 13*

* These differences are not significant.

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Luteinizing Hormone in Persistent Vaginal Œstrus

The placement of experimental lesions in the anterior part of the hypothalamus may be followed by persistent vaginal œstrus in the guinea pig and rat. Such animals possess relatively small ovaries which have no fresh corpora lutea. Various attempts have been made to explain these effects in terms of an altered output of gonadotrophins by the pituitary gland. The original view that the secretion of luteinizing hormone was blocked[1] was supported by Van Dyke *et al.*[2], who found that in animals with persistent œstrus induced by lesions, the ovarian interstitial tissue showed a high lipid content indicative of deficiency in luteinizing hormone. Recently, Taleisnik and McCann[3] reported a pituitary luteinizing hormone content in animals with persistent œstrus which was lower than in intact animals. However, after gonadectomy the amount of luteinizing hormone of persistently œstrous rats showed an increase, but the level of hormone in plasma remained low, indicating that the pituitary release of the hormone is blocked. On the other hand, Hillarp[4] concluded, also on the basis of the condition of the ovarian interstitial tissue, that during persistent œstrus luteinizing hormone was still being secreted in considerable amounts. In other work, the possibility was stressed that in persistent œstrus induced by lesions, secretion of follicle stimulating hormone may be enhanced, because in animals which had been operated during the first two weeks after birth, puberty occurred at an earlier age than in control animals. After puberty, a number of these animals showed persistent œstrus[5]. A third possibility has been advanced by D'Angelo and Kravatz[6], who assumed that in persistently œstrous rats secretion of follicle-stimulating hormone may be decreased. This assumption was based on their finding that the serum of unilaterally gonadectomized

Table 1

Donor rats	Regular cycles: Persistent œstrus	Early di-œstrus	Late di-œstrus	Pro-œstrus	Œstrus
	A	*B*	*C*	*D*	*E*
Recipients:					
No. of animals	21	16	16	5	11
Body-weight (gm.)	50·4 ± 0·9	50·5 ± 0·8	50·6 ± 1·5	50·8 ± 1·2	51·4 ± 1·5
Ventral prostate (mgm.)	20·0 ± 1·52	14·2 ± 0·53	19·0 ± 1·80	15·8 ± 1·03	14·4 ± 0·93
Both testes (mgm.) ± *S.E.*	189·2 ± 9·2	157·2 ± 7·3	184·9 ± 10·0	137·8 ± 21·8	147·2 ± 11·9

Student's *t*:	Prostate weight	Testes weight
A—*B*	3·61	2·60
A—*E*	3·14	2·72
A—*C*		1·76
B—*C*	2·56	0·92
C—*E*	2·27	1·12

rats with persistent œstrus contained less follicle-stimulating hormone than that of cycling animals after removal of one ovary.

There is no conclusive evidence for any of these hypotheses. Cook[7] was unable to detect differences between separate pituitary contents of follicle-stimulating and luteinizing hormone when the pooled glands of rats with persistent œstrus were compared with those of intact or operated rats with regular cycles.

We are investigating gonadotrophin contents in pituitary gland and serum of rats with persistent œstrus following a basal lesion in the anterior part of the hypothalamus; the lesions involved the dorsal and caudal end of the optic chiasm. This preliminary report concerns results on pituitary luteinizing hormone. Assays were carried out in the following manner. Individual pituitary glands were homogenized in saline solution with a Potter–Elvehjem apparatus, the final volume of each homogenate being 12 ml. Twice daily 0·5 ml. of each homogenate was injected beneath the skin into one hypophysectomized immature male rat (body-weight 30–40 gm.) for six days, resulting in a total dose of 0·5 equivalent of one single hypophysis. The weight of the ventral prostate served as an index of the luteinizing hormone potency of the pituitary homogenate. The control group consisted of twenty-five rats with a lesion which showed normal cycles, and twenty-three intact rats. Since no differences were apparent between the results obtained in these two categories they were combined in this work. Gans and De Jongh[8], using a slightly different method for assay of luteinizing hormone, have found that pituitary luteinizing hormone fluctuates during the œstrous cycle with a peak during late di-œstrus followed by a decline in pro-œstrus. In the present work, therefore, the data on control rats were related to the phase of the œstrous cycle prevailing at the time of death. The finding of Gans and De Jongh was confirmed as may be seen from Table 1. Animals with persistent œstrus possessed a high pituitary luteinizing hormone potency, comparable with that noted in the late di-œstrus phase of the normal cycle. Both the weights of the ventral prostate and of the testes of recipients of pituitary homogenates derived from these two groups of individuals were significantly higher than those of recipients of homogenates obtained from rats in œstrus or early di-œstrus.

These findings show that a hypothalamic lesion causing persistent œstrus and inhibition of ovulation does not necessarily block the production of luteinizing hormone within the pituitary gland. The high pituitary content may be the result of an enhanced production or an inhibited release of luteinizing hormone. It is of great interest that preliminary results on serum luteinizing hormone have brought to light a marked contrast between the conditions of persistent œstrus and late di-œstrus; while the high pituitary luteinizing hormone content of late di-œstrus has a parallel in the high serum content, the serum of rats with persistent œstrus possesses luteinizing hormone in only barely detectable amounts. If the latter finding can be confirmed, it would seem that a hypothalamic lesion which does not necessarily affect production of luteinizing hormone may inhibit its release from the gland.

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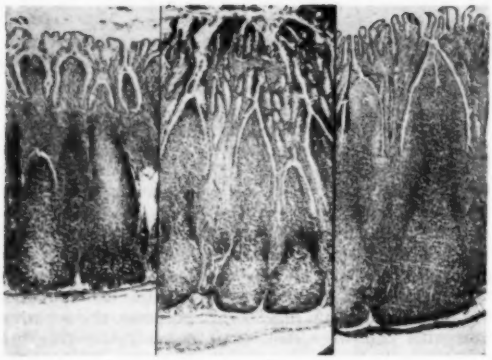
Morphological Changes following Transplantation and Chronic Obstruction of the Rabbit Appendix

Experiments reported by Sholpo[1] from the Moscow Medical Institute are claimed to be evidence in support of the theory that morphology and function depend on environment. In a series of 46 animal experiments Sholpo transplanted the rabbit cæcal appendix to various sites in the small bowel, almost all in the ileum. After three months the transplanted appendices showed marked reduction in the size of the lymphoid tissue. The results were summarized as follows:

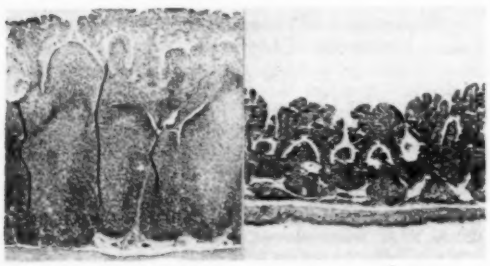
"The vermiform appendix appears to be a convenient object for experimental researches on re-activity and plasticity of tissues of the digestive system. When surgically inserted into the digestive tube at different levels of the latter, the appendix finds itself in (an) unusual functional condition. The operation results in a substantial reconstruction of the wall of this organ: the glandular layer develops intensively, the lymphoid layer reduces both in thickness and in numbers of rows of lymph follicles. The appendix of (the) rabbit begins to display considerable muscular activity which is wanting under normal conditions".

It seemed to us unlikely that the changes which Sholpo described could occur as a result of an altera-



a *b* *c*

Fig. 1. The microscopical appearance of the wall of (*a*) the appendix; (*b*) the saccus rotundus and (*c*) an agminate patch. The villi of the glandular layer are on the top, the main thickness is formed by the lymphoid tissue and a thin muscular layer lies beneath



a *b*

Fig. 2. (*a*) A cross-section of the wall of an appendix three months after transplantation to the ileum (experiment 1). There is little change from the normal appendix. (*b*) Appendiceal wall three months after being subject to chronic obstruction (experiment 4). The glandular and muscular layers have increased and the lymphoid layer decreased

tion of environment as there are normally present in the terminal ileum lymphoid structures identical to those of the appendix. Four or five of these so-called 'agminate patches' are present along the anti-mesenteric border of the ileum, and at the ileo-cæcal junction is found a large collection of lymphoid tissue, the saccus rotundus. The similarity of the microscopical structure of these lymphoid areas to that of the appendix is shown in Fig. 1. Their function also is similar[2]. We therefore felt that an environment compatible with the development of an agminate patch was unlikely to result in the structural alteration of the lymphoid tissue in the appendix, yet we too had observed changes similar to those found in Moscow in appendices transplanted into the ileum. However, as we became more practised at performing the anastomosis we found that these changes occurred less frequently, and stenosis at the suture line became less common.

Table 1

Operation	No. of rabbits	Died	Histologically normal after 3 months	Showing marked histological change after 3 months	With obvious anastomotic stenosis
1. Appendico-ileostomy	6	0	5	1	1
2. Appendiceal inter-position	6	0	3	3	2
3. Ileal diversion	6	3	3	0	0
4. Cæcal obstruction	6	0	0	6	—

Four experiments were therefore devised, the first three exactly like those of Sholpo and the fourth providing obstruction without transplantation: (1) The base of the appendix was separated from the cæcum and the tip anastomosed to the ileum. (2) The appendix was used as a replacement for an excised piece of ileum of equal length. (3) The ileal stream was diverted through the appendix into the cæcum by an end-to-end anastomosis. (In each operation the blood supply to the appendix was preserved and the anastomosis performed with 5/0 arterial silk sutures.) (4) In a further six rabbits the appendix was not disturbed but subjected to a chronic obstruction by producing a proximal cæcal stenosis with carbolized tape.

The normal histological appearance following three months transplantation is shown in Fig. 2*a*. After three months of chronic cæcal obstruction the glandular layer had developed, the lymphoid thickness reduced and the muscle thickness increased (Fig. 2*b*). In only one of the four transplanted appendices which showed a structural change was there no demonstrable suture line stenosis and here there appeared to be a functional obstruction as there was hypertrophy of the proximal ileum.

Sholpo's thesis is therefore rejected. The changes he described following appendiceal transplantation are, we suggest, the result of chronic obstruction as a result of the anastomosis and not the result of altered environment.

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Increased Iron Absorption without Increase in the Rate of Erythropoiesis

It is generally agreed that under normal conditions in man the total body iron is maintained at a relatively constant level by some mechanism which regulates the amount of iron absorbed from the gastro-intestinal tract. Apart from manipulating intra-luminal conditions within the intestine, numerous experimental conditions are known which increase iron absorption and which have in common an accelerated erythropoietic rate. These include anoxic hypoxia[1], cobalt administration[2], erythropoietin administration (Mendel, G. A., unpublished observations), pyridoxine deficiency[3], acetyl phenylhydrazine induced hæmolytic anæmia[4] and anæmia induced by loss of blood[5]. The rate of erythropoiesis has been considered of major importance under 'physiological' conditions in regulating iron absorption[6,7]. In certain disease states, such as hæmochromatosis, however, iron absorption may be increased without measurable increase in erythropoietic rate[8]. It is the purpose of this preliminary communication to report an experimental condition in which gastro-intestinal iron absorption is increased above normal in the virtual absence of erythropoiesis.

Erythropoiesis in the bone marrow of young adult *CF* No. 1 female mice was greatly reduced by the

Table 1. Effect of Hypoxia on Iron Absorption and Erythropoiesis in Normal and Splenectomized Mice treated with Strontium-89

Treatment	Percentage of iron-59 absorbed from gastro-intestinal tract (72 hr.)	Percentage of intravenous administered iron-59 incorporated into red blood cells (24 hr.)	Average reticulocyte count at time of iron-59 administration (per cent)
Normal controls	15·5 ± 3·98 (8)	38·8 ± 2·57 (8)	4·4
Splenectomy strontium-89	11·6 ± 1·32 (10)	4·1 ± 0·36 (6)	0·2
Normal hypoxic	33·1 ± 1·93 (10)	56·5 ± 4·85 (6)	4·2
Splenectomy strontium-89 hypoxic	30·3 ± 4·48 (8)	4·0 ± 0·02 (6)	0·1

No. of animals in each group in parentheses.

* Standard error of mean.

intraperitoneal administration of 4 μc./gm. of strontium-89_{2+} chloride. Jacobson[9] has shown that animals so treated rapidly develop compensatory ectopic erythropoiesis in the spleen. For this reason splenectomy was performed on the day prior to the administration of strontium-89. Eleven days after injection of strontium-89, the rate of erythropoiesis as measured by the incorporation of 1 μc. of intravenously administered ferric iron-59 citrate into red cells was reduced from the normal of 38·8 per cent to 4·1 per cent (Table 1). Reticulocyte values were correspondingly reduced. The gastro-intestinal absorption of 1·5 μc. of force-fed ferrous iron-59_{2+} sulphate was measured, as previously described[2], using total body counting in a Geiger–Müller well counter. Iron absorption was somewhat reduced from the normal value of 15·5 per cent to 11·6 per cent in the splenectomized animal treated with strontium-89. It should be noted that in these experiments iron absorption was measured over a 3-day period to allow time for the elimination of unabsorbed radioiron from the gut. The incorporation of intravenously administered iron into red cells was measured during the 24-hr. period coinciding with time of maximum iron absorption[2].

The influence of hypoxic anoxia on the gastro-intestinal absorption of iron-59 sulphate was studied in groups of normal and splenectomized mice injected with strontium-89. Hypoxia was produced by placing the animals in a chamber in which a gas mixture containing 10 per cent oxygen was maintained. Twenty-four hours after being placed in the hypoxia chamber, intravenous or intra-gastric iron-59 was administered. Twenty-four hours later, the animals were removed from the chamber. Normal mice made hypoxic showed a marked increase in iron absorption (33·1 per cent) as well as an increase in erythropoietic rate (56·5 per cent) (Table 1). The splenectomized mice treated with strontium-89 that were made hypoxic likewise showed a marked increase in iron absorption (30·3 per cent) but no increase in the rate of erythropoiesis (4·0 per cent).

Mazur[10] has presented evidence that the transfer of iron from liver ferritin to the plasma under hypoxic conditions in rabbits, guinea pigs and dogs is mediated by the enzyme xanthine oxidase. The present demonstration of increased iron absorption independent of increased utilization of iron by the bone marrow under hypoxic conditions suggests that a similar enzymatic mechanism may be of importance in the regulation of iron absorption. The hypoxic splenectomized animal injected with strontium-89 should provide a useful model for the study of enhanced iron absorption that is independent of accelerated erythropoiesis. The details of these experiments as well as related studies will be reported at length elsewhere.

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PHARMACOLOGY

Hypertensive Effects of Bradykinin in Rats

Bradykinin obtained from ox plasma[1] and synthetic bradykinin cause intense vasodilatation in many mammalian species. Intravenous injections of bradykinin lower arterial blood pressure in anæsthetized animals. On a molar basis, bradykinin is only ten times less active than acetylcholine and as active as histamine[1]. Two crude bradykinin-containing extracts from ox plasma—one prepared by us and the other kindly supplied by Prof. Rocha e Silva—were shown to have the typical depressor action in normal rats, but frequently produced a striking hypertensive effect in rats nephrectomized 16–24 hr. before. These results are similar to those obtained with anephrotensin prepared from rat serum[2].

It seemed of interest to investigate whether pure bradykinin has the same hypertensive action in nephrectomized rats as the crude extract. Forty-six male rats (180–200 gm.) were nephrectomized under brief bromethol anæsthesia; 8–24 hr. later they were again anæsthetized with allobarbitone and their blood pressure recorded from a carotid by a membrane manometer. Twenty-four sham-operated animals were used as controls. Synthetic bradykinin (Sandoz) supplied in sterilized ampoules, and a natural (89 per cent) purified product prepared by Dr. Elliott were diluted with Tyrode solution and injected into a femoral vein. Three ranges of dose were used (μgm./100 gm. body-weight): low (0·005–0·1), medium (0·15–0·5) and high (0·55–6·0). Angiotensin-amide (5-valyl) and anephrotensin were tested in the same animal. Anephrotensin was obtained from the serum of dogs nephrectomized 48 hr. before; 0·005–0·1 ml. of the purified extract was given intravenously.

In the intact rat with normal blood pressure (110–130 mm. mercury) pure bradykinin, whether natural or synthetic, decreased arterial pressure. Occasionally a small rise followed the hypotensive response. In nephrectomized rats three different types of response were observed: (*a*) a rise in blood pressure; (*b*) a rise in blood pressure preceded by a transient and slight drop; and (*c*) a weak depressor effect, which was usually less pronounced than the effect of the same dose in a normal rat.

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The type of response obtained depended both on the level of arterial pressure at which the injection was given and on the dose. Out of a total of 61 injections of 'low' doses given to nephrectomized rats with an arterial blood pressure less than 100 mm. (60–100 mm.), 62 per cent purely hypertensive, 36 per cent diphasic and 8 per cent hypotensive responses were obtained. The incidence of hypertensive effects decreases when higher doses are used. But when low and medium doses were injected into nephrectomized rats with blood pressures of 60 mm. or less, a hypertensive effect was observed in all instances. In nephrectomized rats with high arterial pressures (100–140 mm.), a hypertensive effect of low doses of bradykinin was observed in 31 per cent and after medium doses in 17 per cent.

When intact rats (in which bradykinin is uniformly hypotensive) were treated with a ganglion-blocking drug such as pentolinium, bradykinin produced a hypertensive effect in 76 per cent and a diphasic response in 24 per cent. In rats with low blood pressure due to pentolinium, bradykinin had a hypertensive effect in all instances.

These results in anæsthetized rats show that the hypotensive action of bradykinin is converted into a hypertensive one when basal pressure is lower than usual. This was seen in nephrectomized animals investigated 8–24 hr. after removal of the kidneys and in intact rats treated with pentolinium; a purely hypertensive action of bradykinin is more frequently observed with small doses. The hypertensive action of bradykinin seems to be more dependent on the initial level of the blood pressure than on the absence of the kidneys. In contrast, dog anephrotensin produces stronger hypertensive effects in nephrectomized rats than in normal animals, irrespective of the initial blood pressure.

The fact that low and medium doses of bradykinin in pentolinium-treated or nephrectomized rats cause hypertensive effects will have to be taken into account when such animals are used in tests for angiotensin in extracts of blood which contain bradykinin.

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Release of Noradrenaline from the Spleen of the Cat by Acetylcholine

Acetylcholine contracts the spleen of the dog[1] and cat[2]. In these species the effect of acetylcholine in contracting the spleen is not blocked by atropine, but is blocked by dibenzyline and reduced by prior treatment of the animal with reserpine; thus it appears that the action of acetylcholine may be mediated by releasing noradrenaline from its stores in the spleen, which afterwards causes a contraction. The work reported here provides further evidence that acetylcholine liberates noradrenaline from the cat spleen.

The cat spleen was prepared for the collection of samples of its venous blood by a method similar to that in ref. 3, in which a large vein branching from the main splenic vein was cannulated. In addition a branch of the splenic artery was cannulated to permit intra-arterial injections into the spleen. Heparin was given intravenously. The splenic nerves were divided to exclude the reflex liberation of noradrenaline. Acetylcholine bromide (1·5 mgm.) was diluted with the animal's own plasma immediately before use, and injected into the splenic artery. Splenic venous blood was collected during the next 40-sec. period by temporarily occluding the main splenic vein, so diverting the flow through the cannulated branch; the blood was centrifuged and the plasma stored at − 10° C. until required for assay. Control samples of plasma were collected before acetylcholine injections. Plasma noradrenaline was assayed on the blood pressure of the pithed rat recorded with a strain-gauge transducer as described in ref. 4. The acetylcholine in the plasma was assayed on the blood pressure of the cat, to see whether there was sufficient to interfere with the assay for noradrenaline. It was found that the volume of plasma injected into the rat contained less than 2 μgm. of acetylcholine. As a further precaution against acetylcholine interfering with the noradrenaline assay the pithed rat was injected with 1 mgm. of atropine and 1 mgm. of hexamethonium. This treatment blocked both the muscarinic and nicotinic effects of 1 mgm. of acetylcholine.

Table 1. Effect of Acetylcholine (1·5 mgm.) injected into the Splenic Artery on the Noradrenaline Content (mgm./ml.) of Venous Plasma from the Cat Spleen before and after Phenoxybenzamine (10 mgm./kgm.)

	Before phenoxybenzamine			After phenoxybenzamine		
Cat No.	Control	After acetylcholine	Increase	Control	After acetylcholine	Increase
1	30	30	0	30	50	20
2	60	100	40	80	170	90
3	50	50	0	50	75	25
4	7·5	10	2·5	10	20	10
5	15	15	0	15	25	10
6	30	30	0	35	70	35
7 (reserpine-treated)	10	8	−2	7·5	7·5	0
8 (reserpine-treated)	20	20	0	12	12	0

The results are summarized in Table 1. The injection of acetylcholine into the splenic artery produced contraction of the cat spleen, but only in two out of six experiments was this accompanied by a detectable increase in the noradrenaline content of the splenic venous plasma.

Brown and Gillespie[3] found that phenoxybenzamine (dibenzyline) increased the amount of noradrenaline which appeared in the venous plasma after stimulating the splenic nerve, therefore phenoxybenzamine (10 mgm./kgm.) was injected intravenously into the cats. After phenoxybenzamine the injection of acetylcholine did not contract the spleen, but the amount of noradrenaline appearing in the venous plasma was increased in every experiment. This observation provides a parallel with the experiments of Brown and Gillespie[3], who found an increased output of noradrenaline into the splenic vein after splenic nerve stimulation in the presence of phenoxybenzamine. They suggested that phenoxybenzamine prevented the access of noradrenaline to receptor sites so that more was detected in the venous blood. However, phenoxybenzamine also has anticholinesterase activity[5]. An anticholinesterase would increase

the effect of injected acetylcholine in releasing noradrenaline, and the effect of nerve stimulation if acetylcholine were an intermediary in the release of noradrenaline produced by sympathetic nerve stimulation. Evidence for such an intermediary action of acetylcholine in the sympathetic nerves to the spleen has recently been obtained[2].

Two cats were pre-treated with reserpine as described in ref. 6 in order to deplete the spleen of noradrenaline. In these cats acetylcholine did not produce a contraction of the spleen, nor did it cause an increase in plasma noradrenaline either before or after phenoxybenzamine.

These experiments show that the intra-arterial injection of acetylcholine releases noradrenaline from the spleen of the cat. When the noradrenaline stores were depleted by reserpine the intra-arterial injection of acetylcholine failed to increase the noradrenaline content of the splenic vein blood. These observations provide evidence that the sympathomimetic effect of acetylcholine on the spleen is due to release of noradrenaline from stores within the spleen.

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Protection by Antioxidants against Lethal Doses of Carbon Tetrachloride

Rees, Spector and Sinha[1] have shown that 'Phenergan', 10-(2-dimethylamino-isopropyl) phenothiazine hydrochloride, protects against necrosis of liver cells in rats dosed with carbon tetrachloride. Afterwards, Gallagher and Rees[2] found that 'Phenergan' maintained normal concentrations of oxidized pyridine nucleotides in the liver despite the administration of carbon tetrachloride. These findings, together with those of McLean[3,4] and Gallagher, Gupta, Judah and Rees[5] that 'Phenergan' protects rats against liver necrosis due either to vitamin E deficiency or to administration of thioacetamide, suggested that 'Phenergan' operates on a general metabolic mechanism involved in the maintenance of cellular and mitochondrial integrity. The value of 'Phenergan' as an alternative to vitamin E indicated that its action might be associated with antioxidant properties. Therefore, the antioxidants[6,7] α-tocopherol, sodium selenite and *NN*[1]-diphenyl-*p*-phenylenediamine were investigated as possible protective agents in carbon tetrachloride poisoning.

Female Wistar rats weighing 150–180 gm. were used. They were observed for 14 days after carbon tetrachloride had been administered.

(*a*) *Vitamin E.* Table 1 shows that 95 I.U. of α-tocopherol acetate administered intraperitoneally 40 hr. before 4 ml. of undiluted carbon tetrachloride/kgm. was given by stomach tube protected all of 15 rats against death. The death-rate was also reduced

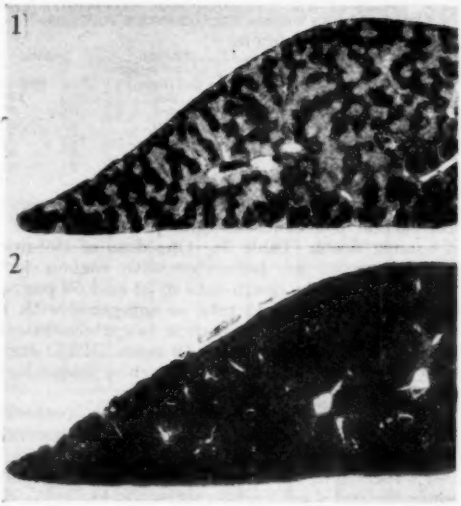

Fig. 1. Sections of liver stained with hæmatoxylin and eosin. (× 5). (1) Rat killed 24 hr. after receiving 4 ml. carbon tetrachloride/kgm. by stomach tube; the section shows widespread centrilobular necrosis and fatty change. (2) Rat killed 24 hr. after receiving 4 ml. carbon tetrachloride/kgm. by stomach tube. The animal had been given 100 mgm. DPPD in 0·3 ml. arachis oil intraperitoneally at 48, 24 and 0 hr. before carbon tetrachloride; the histology is almost normal

by administering 2 doses of 95 I.U. vitamin E at 24 and 6 hr. before carbon tetrachloride. Doses of 95 I.U. given with, and 5 hr. after, carbon tetrachloride were of negligible protective value. A smaller dose (19 I.U.) of α-tocopherol given daily for 3 days prior to administering carbon tetrachloride reduced the death-rate to 72 per cent of 18 rats as compared with 98 per cent of 43 rats given carbon tetrachloride only.

(*b*) *Sodium selenite.* Intraperitoneal injections of 0·5, 0·25, 0·25 and 0·25 mgm. sodium selenite at 72, 48, 24 and 6 hr. before the administration of 2·7 ml. carbon tetrachloride/kgm. reduced the death-rate to 51 per cent of 18 rats as compared with 89 per cent of 18 rats given this dose of carbon tetrachloride only (Table 2).

(*c*) *NN*[1]*-diphenyl-p-phenylenediamine* (DPPD). Three intraperitoneal injections of 100 mgm. DPPD

Table 1. Effect of α-Tocopherol in the Prevention of Carbon Tetrachloride Poisoning

No. of rats	Treatment with α-tocopherol Time (hr. before or after carbon tetrachloride)	Dose (I.U.)	Carbon tetrachloride (ml./kgm.)	Deaths No.	Per cent
43	—	—	4·0	42	98
15	−40	95	4·0	0	0
10	−24, −6	95	4·0	6	60
15	0	95	4·0	12	80
15	0, +5	95	4·0	13	87
18	−72, −48, −24, −6	19	4·0	13	72

Table 2. Effect of Sodium Selenite in the Prevention of Carbon Tetrachloride Poisoning

Group	No. of rats	Treatment with sodium selenite Time (hr. before carbon tetrachloride)	Dose (mgm.)	Carbon tetrachloride (ml./kgm.)	Deaths No.	Per cent
1	18	—	—	2·7	16	89
2	18	72	0·5			
		48	0·25			
		24	0·25			
		6	0·25	2·7	10	51
3	18	72	0·5			
		48	0·25			
		24	0·25			
		6	0·25	—	0	0

Table 3. Effect of *NN*'-Diphenyl-*p*-phenylenediamine in the Prevention of Carbon Tetrachloride Poisoning

No. of rats	Treatment with DPPD Time (hr. before carbon tetrachloride)	Dose (mgm.)	Carbon tetrachloride (ml./kgm.)	Deaths No.	Deaths Per cent
32	—	—	4·0	32	100
19	48, 24, 0	100	4·0	0	0
11	48	100	4·0	6	55
17	0	100	4·0	10	59
12	48, 24, 0	50	4·0	8	67
11	48, 24, 0	10	4·0	7	64

in 0·4 ml. arachis oil at 48, 24 and 0 hr. before giving 4 ml. carbon tetrachloride/kgm. protected all of 19 rats against death (Table 3). One dose of 100 mgm. DPPD either 48 hr. before or with carbon tetrachloride reduced the death-rate to 55 and 59 per cent respectively of 11 and 17 rats, as compared with 100 per cent of 32 rats given carbon tetrachloride only. Courses of 3 injections of 50 or 10 mgm. DPPD during the 48 hr. prior to administering carbon tetrachloride also reduced the death-rate.

The photomicrographs illustrate the protective effect of DPPD against histologically observable damage to the liver by carbon tetrachloride. Fig. 1 shows a section of the liver of a rat killed 24 hr. after having received 4 ml. carbon tetrachloride/kgm. The liver is typical for rats with severe acute carbon tetrachloride poisoning, showing centrilobular necrosis and fatty change. This contrasts with the virtually normal appearance of the liver section in Fig. 2, which is typical for rats killed 24 hr. after the same dose of carbon tetrachloride but which have been given 3 intraperitoneal injections of 100 mgm. DPPD during the 48 hr. before administration of carbon tetrachloride.

It seems likely that the antioxidants protect rats against the lethal effects of large doses of carbon tetrachloride by acting on a general permeability mechanism, and thus prevent the loss of mitochondrial and cellular pyridine nucleotides which would otherwise result from the physical damage to the cell produced by carbon tetrachloride.

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HÆMATOLOGY

Thromboplastic Activity of Red Cells

The problem concerning the relationship of the thromboplastic activity of red cells to that of platelets which Inglis and Halliday[1] have recently studied has, in part, been answered by the work of my associates and me.

It was repeatedly noted that in very mild hæmophilia the prothrombin consumption carried out by my original method was often normal when whole blood was clotted, but not when the platelet-rich plasma was clotted under otherwise identical conditions[2]. This observation led to an investigation of the clotting factor in red cells and its probable role in the generation of thromboplastin. It was found that the activity of hæmolysed erythrocytes (hæmolysate) is similar to that of platelets but quantitatively much greater[3,4]. It is significant that, when a concentrated extract of platelets is added to normal native platelet-poor plasma that has been in contact only with silicone-coated surfaces, the consumption of prothrombin is too small to be determined; whereas, when the plasma is first brought in contact with a glass surface or treated with a minute amount of thrombin, the addition of a platelet extract brings about good consumption of prothrombin[5]. In marked contrast, the addition of an extract of red cells results in a high consumption of prothrombin even when added to native plasma that has been exposed only to silicone-coated surfaces[6].

These findings suggest that platelets can enter the coagulation reaction only after a plasma factor has been activated. Because this activation can occur by exposure to glass, the agent has been designated 'contact factor'. It appears that a platelet constituent interacts with the activated contact factor and that the resultant product is either very similar to, or identical with, the clotting agent found in the red cell. The latter factor, which appears to be a phospholipid[7], does not require contact factor to enter into the clotting reaction. From recent work it appears that some of the clotting agent formed from the platelets during clotting is removed by the red cells[8].

Whether the clotting activity of the intact red cell, which is feeble, has physiological significance remains unanswered. The alternative view that the red cell may be constantly removing this potent agent, which perhaps is being produced continuously, also deserves recognition and consideration.

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We freely acknowledge the priority of Prof. Quick in discovering and reporting the platelet-like thromboplastic activity of red-cell hæmolysate. No reference was made to his work, as it was our opinion that it would be well known to all workers in this field.

The activity reported by us is, however, manifested by non-hæmolysed cells. According to previous reports, non-hæmolysed red cells are capable of exerting only feeble platelet-like activity. Prof. Quick concurs with this. Our work, however, has shown that this is true only in regard to the initial stages of coagulation, but that after the formation of fibrin becomes evident red cells which are still intact develop much greater activity. We have not, as yet, investigated whether this is due to the envelope of the red cell being attacked by thrombin. The activity may be due to the same element in the red cell as is responsible for the platelet-like activity of red cell hæmolysate; but if so, this element can act while still attached

to an intact cell, provided that its activity is released by coagulation initiated in some other way. This activity is not manifested in the prothrombin consumption test described by Prof. Quick because the clot is separated by centrifugation, which also effectively removes the red cells. That centrifugation has this effect also demonstrates that the activity observed is not due to red cells which have been hæmolysed. Some of our recent observations tend to show that, prior to the red cell developing this activity, it has a contrary inhibitory effect. This is in agreement with findings reported by Prof. Quick.

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P_1 Antigen in the Human Fœtus

It is well established that in the human fœtus and new-born the P_1 antigen is incompletely expressed[1,2]. In the course of testing blood from 403 fœtuses between the ages of 12 and 28 weeks we have confirmed that the incidence of P_1 is below the adult-level; however, it was found to be considerably higher in young than in old fœtuses. Moreover, in the early fœtuses the strength of the agglutination also tended to be greater.

Table 1

Crown-rump length	P_1^+	P_1^-	Total	Percentage P_1^+
Less than 10 cm.	50	36	86	58·14
More than 10 cm.	67	250	317	21·14
Adults (ref. 3)	1,984	641	2,025	75·58

Taking a dividing line at 10 cm. it can be seen from Table 1 that the distinction between these two groups of fœtuses is highly significant.

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IMMUNOLOGY

Selective Secretion of Circulating Antibodies in the Milk of the Rat

Passive immunity is transmitted from mother to young in the rat, as in the mouse[1], partly before birth, but chiefly after birth by way of the milk and the gut of the suckling. Postnatal transmission continues until the twentieth day of age[2], when the capacity of the gut of the young rat to absorb antibody terminates although antibody continues to be secreted in the milk. The lactating female rat was chosen for investigating the transmission of antibody from the circulation to the milk.

Table 1. Correlation Tables of Milk Whey and Serum Titres of Rats after Primary (*A*) and Secondary (*B*) Immunization

A

Milk whey titre \ Serum titre	1/1	10	20	40	80	160	320	640	1,280	2,560
1/1,280					1	4				
640						1	3			
320					6	7	5			
160					9	10	3	3		
80			2	9	2	6	5	3		
40			4	5	6	2	1	1		
20				1	2	1	1			
10				1		1				

B

Milk whey titre \ Serum titre	1/1	10	20	40	80	160	320	640	1,280	2,560
1/1,280										
640										
320							1	2		
160						1	10	6	2	2
80						4	13	2		
40				1	3	9	5			
20			1	4	10	1	1			
10			6	2	1					

Female rats were actively immunized within a day or two of the first littering with *Brucella abortus*. Two injections, one of 0·5 and another of 0·75 ml. of the World Health Organization standardized *Brucella abortus* agglutination concentrate, washed and resuspended in a five-fold dilution in saline, were given two days apart subcutaneously in the neck region. Paired samples of blood and milk were collected daily, or on alternate days, and the serum and milk whey titrated in parallel. The same procedure was repeated at the termination of subsequent pregnancies of these same animals.

Antibody appeared in the serum five days after the primary immunization and by the ninth day had attained titres of 1/160–1/640. Thereafter the titres declined gradually to 1/40–1/80 by the end of the first lactation and were at or near this level at the time of each subsequent immunization. The secondary response was more variable: the majority of animals had attained comparable serum titres of 1/160–1/320, while a few animals showed titres of 1/640–1/2,560, by the seventh day.

The appearance of antibody in the milk was strikingly different after primary, as compared with subsequent, immunizations. After primary immunization antibody appeared in the milk one or two days later than in the serum, and by the tenth day reached maximum titres equalling or exceeding those in the

serum. Thereafter these declined more rapidly than in the serum. After secondary immunization the milk titres did not rise appreciably, as did the serum titres, and remained nearly constant throughout lactation, seldom equalling and never exceeding the serum titres. This difference in the ratio of milk to serum titres is shown clearly by comparing the data in *A* with *B* in Table 1. Evidently the antibody formed in response to a primary immunization appears in the milk much more readily than the antibody formed afterwards.

It has been known since the pioneer work of Ehrlich[1] on mice that circulating antibodies, whether actively or passively acquired, do appear in the milk. If it were assumed that the antibody was derived exclusively from that in the circulation, as seems probable, then that which was produced in response to primary immunization was transmitted more readily than that synthesized later. This interpretation involves a selective transmission to the milk of certain molecular types of antibody in preference to others. The only alternative interpretation would require the assumption of local production and direct secretion into the milk of antibody in response to the primary subcutaneous injection of antigen in the neck region, for which there is no evidence.

Selective transmission of antibodies and of labelled globulin has been demonstrated repeatedly in recent years across the fœtal membranes and is known to occur in the guinea pig[2], rabbit[4], monkey[5] and man[6]. It occurs across the neonatal gut-wall in the mouse[7], rat[8] and hedgehog[9], though it has not been observed in the ruminants, horse or pig. It occurs also across the yolk-sac wall of the chick[10]. Hitherto, so far as we are aware, it has been recognized only in transmission across the fœtal membranes and the neonatal gut, so that this is the first instance recognized in an adult and in a glandular secretion.

It will be a matter of considerable interest to determine whether the relative rates of transmission of different antibodies from the circulation to the milk of the mother rat correspond to, or are independent of, those across the gut wall of the suckling rat; or whether these two membranes, across which the antibodies must pass in transit from the maternal to the neonatal circulation, exercise selection on a similar or dissimilar basis.

I am much indebted to Prof. F. W. Rogers Brambell for helpful advice and encouragement in this work and Mr. W. A. Hemmings and Dr. R. Halliday for their interest; and to Dr. A. W. Stableforth and Mr. W. T. Rowlands, of the Animal Health Division of the Ministry of Agriculture, Fisheries and Food for supplies of antigen.

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PATHOLOGY

5′-Adenylic Acid Deaminase in Dystrophic Mouse Muscle

The discovery[1], in 1955, of a hereditary myopathy in a strain of mice has provided a useful subject for the investigation of muscular dystrophy. Although the ultimate cause of the mouse disease may not be identical with the cause of any of the human muscular dystrophies, it is a reasonable assumption that many of the secondary changes will be similar. A number of workers have reported quantitative enzyme changes in the dystrophic mouse muscle. Some activities, for example, cathepsins[2] and glucose-6-phosphate dehydrogenase[3], show an increase; others, for example, lactic dehydrogenase[4] and phosphorylase[5], are decreased.

5′-Adenylic acid deaminase, which converts adenosine-5′-phosphate into inosine-5′-phosphate (apparently irreversibly) is known to be present in much higher concentration in skeletal muscle than in any other tissue. Its physiological function is, however, uncertain. The experiments reported here show a sharp decrease in the activity of this enzyme in dystrophic mouse muscle.

Four pairs of female mice, of the Bar Harbor strain, 3–5 months old, were used. The animals of each pair were litter-mates; the 'normal' mice were heterozygous with respect to the recessive gene responsible for the disease. Muscle from the hind limbs was chopped finely and homogenized for 3 min. with about 5 volumes of ice-cold distilled water in a Potter–Elvehjem homogenizer rotating at high speed. The homogenate was kept in ice for about 30 min., and diluted (usually 1 : 50) with distilled water. Suitable volumes were shaken gently at 37° C. for 10 min. in a medium (total volume, 1 ml.) containing citric acid–sodium citrate buffer, *p*H 6·7 (0·1 *M*) and 5′-adenylic acid (sodium salt) (5 μmoles). Perchloric acid (1 ml., 10 per cent) was then added; after centrifuging the sample, the ammonia content of the supernatant was measured with Nessler's reagent. Homogenates produced no measurable ammonia from adenosine under the same conditions.

The reference base was 'non-collagen N', determined by standing samples of the homogenate overnight at 30° C. with 0·1 *N* sodium hydroxide; they were then centrifuged and total nitrogen of the clear supernatant determined by a micro-Kjeldahl procedure. (Such 'non-collagen N' represented on the average about 90 per cent of the total nitrogen of the tissue.)

The results are shown in Table 1. It may be seen that the mean activity of the muscle from the affected animals was only about one-third that of the normals. The activities bore no relation, in either group, to the age of the mice.

Mixtures of homogenates from normal and dystrophic muscle were also tested. The combined activities were equal to the sum of the activities when tested separately, thus making it unlikely that

Table 1. 5′-Adenylic Deaminase Activity in Skeletal Muscle from Dystrophic and Normal Mice

	Ammonia produced (μmoles/mgm. of non-collagen nitrogen)	
	Normal	Dystrophic
	192	51·6
	127	60·8
	217	64·8
	206	54·6
mean	186	57·9

Muscle homogenates were incubated with 5′-adenylic acid as described.

the low activity of the dystrophic muscle is due to an inhibitory factor.

The *p*H-activity curves in citrate buffer for normal and dystrophic muscle were similar, with a peak at 6·7. The relative activity of the two was approximately the same in succinate buffer (*p*H 6·4) as in citrate buffer, although the measured activities were about 25 per cent lower.

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Identification of Antibody in β_2-Globulins of Mouse Serum and Ascitic Fluid

Mice given intraperitoneal injections of antigen–adjuvant mixture[1–3] produce large amounts of ascitic fluid which contains specific antibodies. Inbred *AKR* mice injected intraperitoneally with isologous tumour cell fragments in modified Freund's adjuvant developed large amounts of peritoneal fluid which contained specific cytotoxic and neutralizing antibodies[2,4]. These observations had immediate practical importance since immunological studies have been limited by the small amount of antiserum obtainable from each mouse. Since little or no information on the biophysical properties of mouse ascitic fluid is available, an investigation was made of its electrophoretic and immunological characteristics.

Female *AKR* mice were injected intraperitoneally with: complete Freund's adjuvant; incomplete Freund's adjuvant from which *Mycobacterium butyricum* was omitted; or complete Freund's adjuvant containing isologous lymphoma cell fragments. Female *CF*1 mice were injected with crystalline bovine serum albumin in complete Freund's adjuvant. Complete Freund's adjuvant (85 parts Drakeol mineral oil, 15 parts 'Arlacel A', 1 mgm. of *Mycobacterium butyricum*/ml.) was modified so that the aqueous phase was due only to the water contained in the packed lymphoma cell fragments or crystalline bovine serum albumin. Antigen–adjuvant mixtures with little or no aqueous phase were more effective in causing ascites formation than conventional water-in-oil emulsions. Animals received three 0·25 ml. injections one week apart. Approximately 2 weeks after the last injection ascitic fluid was obtained by paracentesis and blood by cardiac puncture. Serum and ascitic fluid were clarified by centrifugation. Moving-boundary electrophoretic analyses were made in a Spinco model *H* instrument (barbital buffer: *p*H 8·6; $\mu = 0{\cdot}1$). The component containing antibody was identified by the boundary disturbance test[5]. In this procedure antigen is added to the buffer in the electrophoretic cell. Combination of antigen with antibody in a specific component forms a precipitate which interrupts the light and produces a clear area in the electrophoretic pattern. Ascitic fluid was fractionated by starch block electrophoresis (barbital buffer: *p*H 8·6; $\mu = 0{\cdot}075$), and the fractions tested for precipitins by the interfacial ring test.

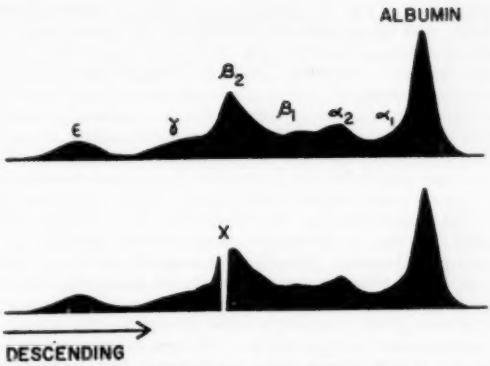

Fig. 2. Electrophoretic boundary disturbance patterns of ascitic fluid from *CF*1 mice immunized with bovine serum albumin. Top, control; bottom, 1 μgm. bovine serum albumin/ml. buffer

Normal *AKR* serum (Fig. 1*A*) consisted of seven discernible components conventionally designated as γ-, β_2-, β_1-, α_2-, α_1-globulin, albumin, and a prealbumin component, ρ. The concentration boundary is designated as ϵ. Comparison of the electrophoretic patterns and analysis of the relative percentage of each component were made. Serum pools and ascitic fluid pools from *AKR* mice injected with complete Freund's adjuvant (Figs. 1*B*, 1*D*) or with complete Freund's adjuvant with lymphoma cell fragments (Figs. 1*C*, 1*E*) had increased relative percentages of α_2- and β-globulins compared with normal serum. The α_2-globulins were in greater concentration in the sera of immunized animals (Figs. 1*B*, 1*C*) than in corresponding ascitic fluids (Figs. 1*D*, 1*E*). The prealbumin component present in all serum pools was not detectable in ascitic fluid.

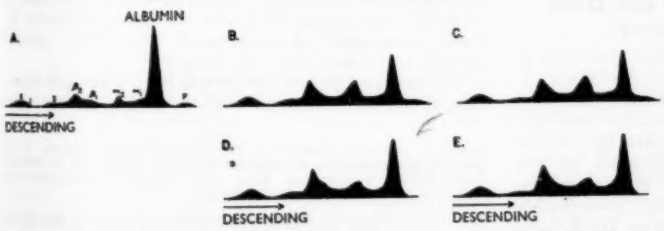

Fig. 1. Electrophoretic patterns of *AKR* mouse sera and ascitic fluids. *A*, Normal *AKR* mouse serum; *B*, serum from mice injected with complete Freund's adjuvant; *C*, serum from mice injected with lymphoma cell fragments in complete Freund's adjuvant; *D*, ascitic fluid from mice injected with complete Freund's adjuvant; *E*, ascitic fluid from mice injected with lymphoma cell fragments in complete Freund's adjuvant

Animals injected with incomplete Freund's adjuvant did not produce ascites. The *Mycobacterium butyricum* component of the adjuvant mixture was necessary for the induction of ascites by the immunization procedure described.

Ascitic fluid from *CF*1 mice contained anti-bovine serum albumin precipitins. A well-defined boundary disturbance (*X* in Fig. 2) was

produced in the β_2-globulin component when ascitic fluid (475 μgm. anti-bovine serum albumin protein/ml.) was treated with 1 μgm. of bovine serum albumin/ml. buffer. Eluates obtained from starch-block electrophoresis of ascitic fluid contained anti-bovine serum albumin precipitins in fractions corresponding to β-globulins. The *CF*1 serum was also shown to contain anti-bovine serum albumin precipitins in the β_2-globulin region by the boundary disturbance method.

Serum and ascitic fluid from *AKR* mice had a similar distribution of electrophoretic components with one major difference. Ascitic fluid did not contain prealbumin. Relative concentrations of α_2- and β-globulins were greater in serum and ascitic fluid from immunized animals than in serum from normal mice; however, there was very little change in the relative concentration of γ-globulin. This raised the question as to which component contained the antibody. Boundary disturbance experiments showed that the anti-bovine serum albumin precipitins of mouse ascitic fluid and serum were contained in the β_2-globulin. Prolonged immunization of the mouse might result in localization of antibody in a serum component other than β_2-globulin.

Mouse serum contains a prealbumin component not detected in ascitic fluid. The relative concentration of α_2- and β-globulins was greater in the serum and ascitic fluid of immunized animals than in the serum of normal mice, whereas γ-globulin remained relatively unchanged. Anti-bovine serum albumin precipitins have been demonstrated in the serum and ascitic fluid of immunized mice and have the electrophoretic properties of a β_2-globulin.

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Nature of Increased Protein and DNA in Chronic Hepatic Injury

Excess protein and deoxyribonucleic acid (DNA) are found in chronic hepatic injury, for example, after administration of ethionine[1–3], butter yellow[4,5], 2 acetyl aminofluorene[6,7], and a high fat–low choline–low protein diet[1]. This suggested that the excess protein or DNA is an abnormal product of the hepatocytes[1–3]. This is supported by the incorporation of ethionine into hepatic proteins[3], presumably the abnormal proteins. These proteins, or DNA, have been related to cancer[1,7]. This communication is to point out that the excess protein formation results from alterations in cell population, rather than from formation of abnormal proteins.

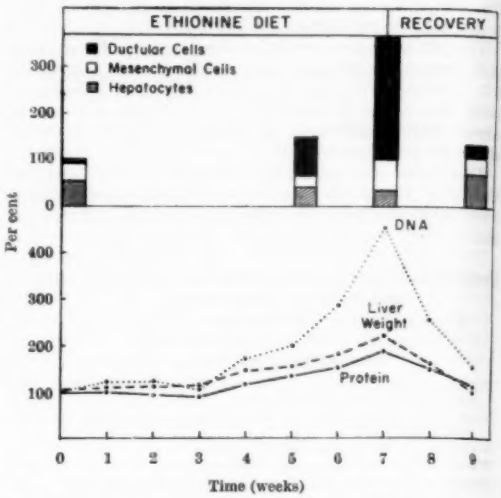

Fig. 1. Changes in liver weight, hepatic protein and DNA content, and cell population during ethionine intoxication

A group of 42 rats was fed a synthetic diet supplemented by 0·5 per cent ethionine, with groups killed weekly up to seven weeks. An additional 12 rats were similarly treated and then placed on the synthetic diet supplemented by 1 per cent methionine. They were killed after one week or two weeks. Twenty rats fed the synthetic diet alone were controls.

From the third to seventh week the liver enlarged and its total protein content nearly doubled (Fig. 1), with collagen (determined as hydroxyproline) accounting for only 5 per cent of the increment. The total DNA content increased almost five-fold, while the RNA/DNA ratio decreased from 4 to 1·8. While in the control liver the ductular cells accounted (on the basis of differential cell counts) for only a small fraction of the population, with a ductular cell: hepatocyte ratio of 1 : 10, after seven weeks on ethionine the ductular cells predominated, the above ratio being 7 : 1. Calculating the change in the total number of cells, the ductular cells increased about 50 times, while the number of hepatocytes decreased slightly (Fig. 1). After two weeks of methionine supplementation, total protein and DNA reverted almost to control-levels, parallel with the disappearance of almost all ductular cells and a restoration of the cytological pattern of the liver. After administration of 0·3 μc. tritiated thymidine/gm. body-weight at the seventh week of ethionine intoxication, incorporation of thymidine determined by scintillation counting was about 30 times the control (Table 1). Radioautographs demonstrated the label almost exclusively in ductular cells (Fig. 2).

The rise in DNA is accounted for by the proliferation of bile ductules, qualitatively and quantitatively,

Table 1. Incorporation of Thymidine-^{3}H into Liver DNA, and the Distribution of Radioautographic Label in Different Cell Types in Control Rats and Rats Intoxicated with Ethionine

Diet	Total activity in DNA c./min.	No. of labelled cells per 100 high-power fields: Hepatocytes	Mesenchymal cells	Ductules
Control	1,760	4	6	3
Ethionine (7 weeks)	47,250	12	18	200

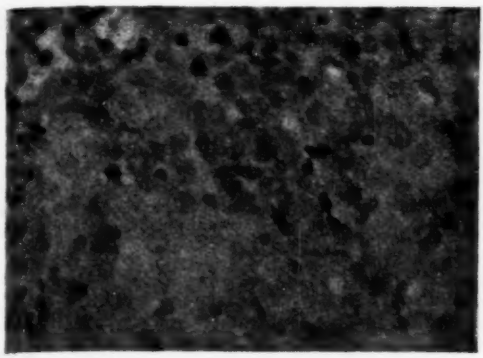

Fig. 2. Radioautograph of liver of rat fed ethionine for 7 weeks and then given tritiated thymidine. Labelled cells are all ductular cells. Hæmatoxylin. (× 120)

as shown by cell counts and autoradiography. Allometric analysis of the individual results for DNA and total protein shows a close relationship, indicating that the increase in liver weight and total protein are functions of proliferation of ductular cells. The smaller rate of increase in total protein and RNA than in DNA is explained by the much smaller cytoplasm to nucleus ratio of the ductular cell. In addition, the disappearance of excess protein and ductules during recovery run parallel. After a high-fat – low-protein diet, bile duct ligation and administration of α-naphthyl isothiocyanate and 2-acetyl aminofluorine, the same chemical and histological relationships hold true.

The excess protein and DNA are thus the structural protein of another cell type pre-existing in the normal liver rather than the accumulation of abnormal proteins as a reflexion of metabolic alterations of the hepatocytes. That the average cell size becomes smaller[5,6] is also explained by the proliferation of this new cell type. Radioautographs demonstrate that the previously observed increased uptake of thymidine-^{3}H (ref. 2) in ethionine intoxication is merely a reflexion of proliferation of ductular cells. No evidence exists that proliferation of ductular cells in the rat is related to carcinogenesis. The correlated approach applied emphasizes the value of morphological controls in the study of liver injury.

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BIOLOGY

Translocated Heat Injury in Plants

Translocated heat injury is common in burns of human beings[1] but is apparently not recorded in plants. When one of the two primary leaves of pinto bean (*Phaseolus vulgaris* L.) or cowpea (*Vigna sinensis* ((Torner) Savi) or the cotyledons of National Pickling cucumber (*Cucumis sativus* L.) was heated in water (5 sec. at 70° C. was suitable) and the opposite leaf abraded as in mechanical inoculation with viruses, the heated leaf was killed and the unheated leaf was severely injured. There was no apparent injury to the petioles and stem through which the injury stimulus passed. When the heated leaf was removed from the plant within 4 hr. after heating, the translocated injury to the opposite leaf was prevented, or recovery was favoured. Translocated injury still occurred if heating followed abrasion by as much as 12 hr., or if abrasion followed heating by as much as 16 hr., but comparable injury never occurred from abrasion or heat only. As the ratio of the area of the heated leaf to that of the unheated leaf was increased by removal of part of the leaf area, translocated injury was increased. The time of day to produce maximum translocated injury quickly was in the morning, but translocated injury could be produced at any time of day. Translocated injury was favoured by light and high temperatures in the environment. As the age of plants was increased from 12 to 23 days the degree of translocated injury was increased. The temperature coefficient for translocated heat injury was about 10. This translocated heat injury had various effects on infections which will be reported elsewhere. While no chemical responsible for translocated heat injury has been demonstrated, these results suggest a similarity between translocated heat injury in plants and animals.

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A Distinction between Bolting and Flowering Effects on Senescence

It is well known that flowering and fruiting processes bring about the senescence of most annual species of plants. Molisch[1] interpreted this senescence as due to the mobilization of food materials into the fruits. His interpretation has been questioned by Leopold, Kamien and Janick[2], for staminate as well as unpollinated pistillate plants of spinach show senescence after flowering. Both staminate and pistillate spinach plants develop a large seed stalk with the commencement of reproductive development, and it may be that Molisch's interpretation could be made more correct by including the mobilization of food materials into the stalk as an explanation of the imposition of senescence. The application of gibberellin to spinach which has not experienced photoperiodic induction will result in the formation of a stalk without the further development of flowers, providing an opportunity for distinguishing between the effects of bolting and of flowering on senescence.

Spinach plants of the 'Spica' variety planted on November 14, 1960, were grown under natural winter day-length. On March 31, 1961, twenty plants were selected for uniformity and divided into four groups of five plants each. Two groups were placed under short days (8 hr.) and two groups under long days (17·5 hr.). Day-lengths were shortened with curtains or lengthened with about 100 ft.-candles of tungsten light. Within each photoperiodic regime, one group was sprayed with 1,000 p.p.m. of gibberellic acid with the other group acting as a control.

Fig. 1. Separation of bolting and flowering effects on senescence in spinach. Treatments from left to right: 1, short day; 2, short day + gibberellic acid; 3, long day; 4, long day + gibberellic acid. Photographed 49 days after treatment

Under conditions of long days, all plants bolted and flowered and afterwards showed senescence. The dates of death of plants treated with gibberellic acid and controls were essentially the same. Four of the ten plants were staminate and died in 33–51 days while the six pistillate plants died in 46–56 days. The final height of the plants treated with gibberellic acid was only slightly greater than the controls. Under the short-day treatment all plants were non-senescent at the end of 46 days, although the treated plants had elongated to an average height of 11 in. (Fig. 1). At this time two plants each from the gibberellic acid treatment and control were transferred from short- to long-day treatment. These flowered in two weeks and all showed normal senescence, the plants dying between 45 and 51 days from this date. Of the six remaining plants left under short days, four were abandoned as a result of insect infestation. The two remaining, one treated and one control, were non-senescent at the end of 74 days, a total of 120 days from the start of the original treatments, at which time the experiment was terminated.

The results demonstrate that the stimulation of an amount of stem growth in vegetative plants comparable with that produced in flowering spinach plants does not produce the stimulus for senescence which the bolting and flowering do. We suggest this as further evidence that the simple mobilization of materials is not the principal cause of senescence following reproduction, for the development of the small staminate inflorescences induces senescence whereas in contrast the growth of the massive central stem of plants treated with gibberellic acid had no detectable effect. For rapid growth of the stalk there must be a large mobilization of food substrates into the stalk and yet the death of the plant does not follow. It would appear that not all mobilizing forces within the plant induce senescence.

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Biosynthesis of Gossypol by Excised Cotton Roots

Gossypol, a toxic phenol, occurs primarily in the resin glands of cotton seed but also has been isolated from the tap-root bark of the cotton plant[1]. A study of the distribution of gossypol in the cotton plant revealed that the roots, especially the feeder roots, contained high levels of gossypol. This was true for strains of cotton in which the plants and seed were free of resin glands as well as for strains which contained many glands in plants and seed. The high levels of gossypol in the roots and the minute amounts in the seed of the glandless plants suggest that the gossypol was synthesized in the root tissue.

Since techniques for the growth of excised root tissue in sterile nutrient solutions have been developed[2,3] it seemed feasible to investigate the biosynthesis of gossypol by cotton root tissue. Excised root tips incubated in a sterile nutrient solution were used to determine if gossypol is synthesized by growing cotton root tissue. Dawson[4] found that excised roots of the tobacco plant synthesized nicotine.

The technique used for the culture of the excised root tissue was similar to that of Robbins with the tomato[3].

Cotton seed from both glanded and glandless strains were delinted with concentrated sulphuric acid and washed well with water saturated with calcium oxide. The seeds were sterilized by suspending them for 5 min. in a 0·5 per cent sodium hypochlorite solution ('Clorox' diluted 1 : 10). The treated seeds were washed three times with sterile distilled water and then transferred to sterile plates containing nutrient agar. The plates were incubated at about 30° C. until the roots had emerged from the seed to a length of 0·5–0·75 in.

The root tips were excised with a sterile razor blade and sampled randomly (Table 1, samples 1*a* and 2*a*) to determine the initial gossypol content. The remaining tips were transferred aseptically to 500-ml. Erlenmeyer flasks containing 150 ml. of sterile nutrient solution. The solution was identical, except for the inclusion of 0·05 p.p.m. of iodine, to that of Robbins[3], which contained the following in mμmoles per litre: thiamine 20, pyridoxine 200 and nicotinamide 200. The flasks were incubated for about 4 weeks. Some of the roots grew well, while others made little or no growth. At the end of the incubation period the roots were washed with water and, after separating the new growth (Table 1, 1*b* and 2*b*) from the original tips (Table 1, 1*c* and 2*c*) that were used to initiate the root culture, were dried. Both of these parts and the tips that were removed as control samples (Table 1, 1*a* and 2*a*) at the time of transfer into the nutrient solution were analysed separately for total gossypol content as I have already described[4].

Table 1. Gossypol Content of Excised Cotton Roots grown in Nutrient Solutions*

No.	Description	No. of cultures	Mean gossypol content (per cent)
	Glanded strain (1)		
1 *a*	Tips at time of transfer		0·080
1 *b*	New growth in nutrient solution	2	2·300
1 *c*	Incubated tips, new growth removed	2	6·320
	Glandless strains (2)		
2 *a*	Tips at time of transfer	2	0·051
2 *b*	New growth in nutrient solution	2	2·018
2 *c*	Incubated tips, new growth removed	2	1·361

* Values are expressed on an air-dried basis

The results of the analyses which are expressed on an air-dried basis are presented in Table 1. The concentration of the gossypol in the root tips (1*a* and 2*a*) at the time of transfer into the nutrient solution was low, although the level in the glanded strains was somewhat higher than that in the glandless strain. During incubation, however, the gossypol content of the original tips (1*c*, 2*c*) increased very markedly. This change was more apparent for the glanded strain, a 78-fold increase, than for the glandless strain. Moreover, the concentration of gossypol in the new root growth (1*b*, 2*b*) was many times higher than that observed in the original root tips at the time of transfer into the nutrient solution.

Thus these results clearly indicate that gossypol was synthesized by the excised root tissue. Furthermore a sample of root tips from the glandless strain that made no growth when incubated in the nutrient solution contained 2·315 per cent gossypol. This observation indicates that the root tips of the cotton plant have the enzyme systems for the production of gossypol even when they make no growth.

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Juvenile Stage in Cultivated Forms of *Brassica oleracea*

Stokes and Verkerk[1] showed that while chilling induces flowering in Brussels sprouts, there was a juvenile stage during which chilling was ineffective. This is reflected in the horticultural practice of overwintering small seedlings derived from an August sowing of Brussels sprouts, which then grow vegetatively for a whole season without flowering. A similar procedure is successfully followed in the cultivation of spring and some autumn and cattle cabbage, suggesting the existence of a juvenile stage in these also, as if the plants, as a result of a too early sowing, are too large (that is, beyond the juvenile stage); winter chilling induces premature flowering (bolting) in the following spring[2,3]. I have, from August sowings, successfully overwintered outside, seedlings of autumn and winter cabbage (3 cultivars), kale (cottagers, hearting, marrow stem and thousand-headed), kohl rabi (4 cultivars), sprouting broccoli (2 white and 2 purple cultivars) and heading winter cauliflower or broccoli (9 cultivars), as well as those of spring cabbage. With all these cultivated forms a high proportion have, when transplanted to permanent quarters either in the October or April following sowing, continued to grow vegetatively, whereas plants from a July sowing all flowered in the spring following. This experience suggests that in all these cultivated types a juvenile stage exists during which chilling in ineffective in inducing flowering.

This feature was even more marked in plants raised from seed of a wild, although perhaps not indigenous, cabbage collected from the Yorkshire cliffs. Plants of this, from a sowing made on July 7, did not flower in the following spring, whereas all the plants from a corresponding sowing of the cultivated forms enumerated above did flower.

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Kinetin-induced Meiotic-Prophase Acceleration and Stasis in *Tradescantia* Anthers cultured on Media Deficient in Sugar

The ability of kinetin to accelerate mitotic division has been demonstrated for *Paramecium*[1], and an apparent effect of accelerating prophase has been inferred from onion root-tip work[2]. That the acceleration may be a direct consequence of a hormonal acceleration of discrete phases of cellular metabolism has been suggested[3,4]. The former workers found that synthesis of deoxyribonucleic acid (DNA) could be induced in tobacco pith tissue by kinetin; the latter found that it increased the activity of deoxyribonuclease and ribonuclease from bean hypocotyls. It is known that indole-3-acetic acid is also required for stimulation of division by kinetin and it has been shown that it is also required for the effect on nucleic acid metabolism[1–4]. In contrast with the stimulation of nuclear and cellular division, most workers have found that in higher concentrations kinetin causes abnormalities of division and eventually mitotic activity ceases.

We planned to determine whether acceleration could be detected in the prophase of meiosis in anthers of *Tradescantia paludosa*, in which the prophase stages investigated (from pachytene and diplotene onwards) are of sufficient duration to do so. The anthers were cultured on a modification of the basic medium used by Taylor[5] in which 4 per cent lactose was substituted for the equivalent of sucrose, to which kinetin at a concentration of 0·25 p.p.m. and/or different sugars were added. This medium provides semi-starvation conditions, in spite of which approximately two-thirds of the meiocytes in an anther proceed through both stages of the meiotic division with regular nuclear products when cultured at 27° C.

It was found that, among a group of fifteen anthers, excised at pachytene or very early diplotene, seven anthers treated with kinetin had advanced to diakinesis or beyond in 24 hr., and one was at late diplotene; six of the untreated anthers from the same buds were at early or mid-diplotene and one at diakinesis. In addition, in a test involving comparisons between the two lobes of an anther, one treated with kinetin, the other not, five of the treated lobes markedly outstripped the control, and only one

showed apparent retardation. We conclude that kinetin accelerates prophase stages beyond pachytene. Since synthesis of DNA in the meiocytes of *Lilium longiflorum* is already completed before this stage[4] but synthesis of ribonucleic acid (RNA) reaches a peak during it, it is suggested that an enhancement of RNA synthesis, as indicated by observation of enhanced ribonuclease activity (ref. 4), may be responsible for this acceleration.

A large number of tests indicated that in anthers cultured for 48 hr. at mid-diplotene, kinetin caused a cessation of kinetic activity during the meiotic process that we have termed 'meiotic stasis' (Fig. 1). The observed pattern ('random stasis'), in which all the stages from diplotene to anaphase 2 have been detected, suggests that the phenomenon is caused by depletion of the cellular energy or substrate reserves, as a result of the accelerated development of prophase. Citrate, when added at a concentration of 83 p.p.m., markedly alleviated this nuclear stasis, and hence it appears probable that energy through the tricarboxylic acid cycle may be more critical than substrate.

Fig. 1. Microsporocytes in stasis (see text) from a mid-diplotene anther cultured for 48 hr. sucrose-deficient medium containing kinetin (× 665)

In describing the inhibition of mitosis in onion root-tips induced by high concentrations of kinetin (1–5 p.p.m.) Guttman[2] mentions binucleate cells, massed prophases and small, dense cells with heavily stained nuclei. These observations coincide quite closely with our own observations of microsporocytes in kinetin-induced stasis. It appears probable that these abnormalities in mitosis also were a result of energy starvation brought about in the root-tips by nuclear acceleration induced by kinetin.

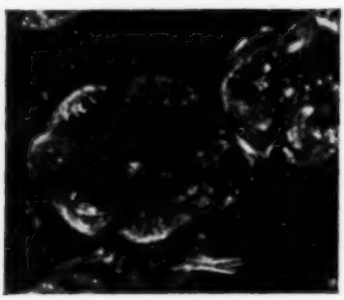

Fig. 2. 8-microspore 'tetrad' produced by an immediate division of the microspore nuclei, from a mid-diplotene anther cultured for 48 hr. on a sucrose-sufficient medium containing kinetin (× 665)

When citrate or sucrose was supplied, mid-diplotene meiocytes in kinetin-treated anthers frequently underwent three successive nuclear divisions within 48 hr. (Fig. 2). In contrast, under natural conditions on the plant, a period of 7 days elapses between the completion of the second meiotic division and the first mitotic division of the microspore[7]. Hence the action of kinetin in this instance apparently involves an elimination of almost the whole of the long intervening metabolic period in the microspores. This would suggest that it controls at least the conditions for the replication of DNA, since in *Tradescantia* microspores the replication occurs at the end of the interphase[8]. This evidence therefore supports that of Patan *et al.*[3] from mitotic work with tobacco pith tissue that the induction of DNA synthesis in the interphase nucleus is a significant feature of kinetin activity.

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Plankton on the North Kenya Banks

During the investigations of the East African Marine Fisheries Research Organization into the resources of part of the coast of East Africa a hitherto uncharted shallow area was located off the north Kenya coast in the vicinity of Lamu[1]. Subsequent investigations have indicated that this area, designated the North Kenya Banks, has a good fish population and is of importance as a potential fishery[2,3].

Due to lack of specialists it has been difficult to make an extended and continuous investigation of the various facets of this marine environment which, together, result in the production of a good fishery. However, during plankton investigations along the East African coast, facts were discovered which substantiate the claim that the North Kenya Banks is a fertile area and potentially a good fishery.

Part of the plankton investigations constituted taking a series of lines of samples from the coast (*c.* 100 fm., or 50 fm. when the fringing reef permitted) outwards for some 40 or 50 miles. These lines of stations were worked from Cape Delgado, near the southern Tanganyika border, to Dick's Head, near the northern Kenya border; the outward lines from the coast were at approximately 30–50-mile intervals. The plankton net used was a Currie and Foxton 70-cm. net[4] without the meter. A filtration coefficient of 1 : 1 has been assumed (reasonable in the light of former experience), in view of the short duration of the haul, the speed of hauling (*c.* 1 m./sec.) and the evident lack of clogging. All were vertical samples from, usually, both 200 m. and 50 m. to the surface at each station. In shallower water the samples were from the bottom to the surface. All samples were duplicated, the first being for numerical and specific analysis, the second for dry weights. These latter

samples were dried to a constant weight at 50° C. in a controlled oven. The resulting weights were applied to the height of the water column from which they were taken, the final result being expressed as mgm./m.³ of sea-water.

Full analysis of the results is not yet complete, but the preliminary results are of much interest. Towards Cape Delgado the plankton dry weight is about 8–12 mgm./m.³, with no great variation in off-shore samples. Farther north in the Mafia area the coastal water is rather richer with *c.* 20–30 mgm./m.³, decreasing to *c.* 8–12 mgm./m.³ in off-shore waters. This trend towards a relatively enriched coastal water increases to the north, and in the Dick's Head area in-shore figures are *c.* 30–40 mgm./m.³, the off-shore figures being *c.* 10–15 mgm./m.³.

A preliminary Survey Report of the 1960 cruise of the Russian research vessel *Vitiaz*, for the International Indian Ocean Expedition, shows the contouring of the plankton dry weight in the top-most 100 m. of the Indian Ocean. It agrees in showing that water with a low plankton dry weight (7·5 mgm./m.³) is much nearer the coast-line in the Cape Delgado area than farther north in the Dick's Head area.

The stations worked over the North Kenya Banks showed the highest figures. Thus, among others, plankton dry weights of 65·1, 55·0 and 62·8 mgm./m.³ were recorded at the bottom end of the range, with the largest reading being 161·6 mgm./m.³. This sample was taken at a depth of 108 m., the position being 2° 25·5′ S. 40° 54′ E.

These readings show that the water over the North Kenya Banks is demonstrably richer than the remainder of the Tanganyika–Kenya coast. Further readings will have to be taken before it can be stated confidently that this applies throughout the year, although there is reason to believe that this is, in fact, the case.

It is worth noting that the colour of the sea over these Banks was the 'bottle-green' associated with such temperate water as the North Sea, and neither the clear blue of the off-shore East African waters nor the dirtier blue or pale greens of the in-shore waters was in evidence.

Of interest is the consideration of the plankton dry weight underneath one acre of water over the North Kenya Banks. Assuming a mean depth of 80 m. and a plankton dry weight of 100 mgm./m.³ the resulting figure is 32·27 kgm. plankton dry weight beneath 1 acre of water.

Analysis of the preserved samples has not yet been completed, but random examinations give every indication of a richer population of fish eggs and larvæ compared with the rest of the coast. This poses the problem, to be investigated later, of whether the North Kenya Banks are a breeding ground, with the fish converging from outlying waters to breed, or whether the North Kenya Banks are mainly a feeding ground, the breeding being resultant and dependent on this.

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CYTOLOGY

Increase in the Dense Cytoplasmic Bodies in Radiation-induced Giant Cells of the Cultured Fibroblast

The formation of giant cells after the irradiation of cell cultures was described by Puck and Marcus[1] in HeLa cells. The phenomenon also occurs in cultured fibroblasts. After a dose of 1,000 r., a high percentage of the cells in the cultures cease to undergo mitosis but continue to grow in bulk, forming characteristic giant cells which survive for about two weeks under normal culture conditions. Dickson, Paul and Davidson[2] have shown that the giant cells contain twice the deoxyribonucleic acid, ribonucleic acid, protein and lipid of the normal cell and that the synthesis of these compounds appears to be normal. The primary radiation effect, therefore, would seem to be on the mechanics of mitosis.

The non-irradiated, mouse subcutaneous fibroblast (strain *L* (ref. 3)) is roughly circular in thin sections under the electron microscope, with a single nucleus and cytoplasm containing typical mitochondria, sparse granular endoplasmic reticulum, a diffuse Golgi apparatus, numerous vesicles and 'dense cytoplasmic bodies'. The last-named are a characteristic feature of these and other cultured cells[4]. They are circular bodies, approximately 0·5 mμ in diameter, with a single outer membrane and opaque ground substance, and occur three or four to a cell in the thin sections. In a few cases the outer membrane is duplicated for part of its length, or even laminated. Rarely, a myeloid body is seen. Other structures are present, the ground substance of which is intermediate in density between that of the dense bodies and that of the cytoplasmic vesicles.

Pinocytosis can be demonstrated easily in these cells by growing them in a medium containing 2 per cent 'Thorotrast' ('Testagar'). After an hour, granules of thorium dioxide are present throughout the cytoplasm on the inner surface of membrane-bound vesicles. A few of the dense bodies also contain one or two granules at this stage. If cells treated with the 'Thorotrast' are returned to a normal medium for a further 24 hr., all the intracellular granules are segregated within the dense bodies which, therefore, correspond to the residual bodies of Palade[5].

In the giant cells developed from the fibroblasts after irradiation, the nucleus is large and convoluted so that thin sections often give an impression, seldom confirmed on light microscopy, of multi-nucleation. Individually the cytoplasmic structures are identical with those of the non-irradiated cells, though the Golgi apparatus may appear more diffuse. The striking feature of these cells, however, is the increase in the number of the dense bodies, which occur in groups of 12–15 in each cell in the thin sections. As in the normal cell, they are approximately 0·5 mμ in diameter, with a smooth outer membrane and opaque ground substance. Their internal structure is more variable, most have some lamellations and myeloid bodies are fairly common. After 'Thorotrast' treatment for 1 hr., the dense bodies of the giant cells, in contrast to those of the normal cells, show a considerable concentration of granules (Fig. 1). 'Thorotrast'-treated giant cells, returned to a normal medium for a further 24 hr. show the substance to be entirely localized in the dense bodies.

It is concluded that, as a result of continuous pinocytosis, when cell division in cultured fibroblasts

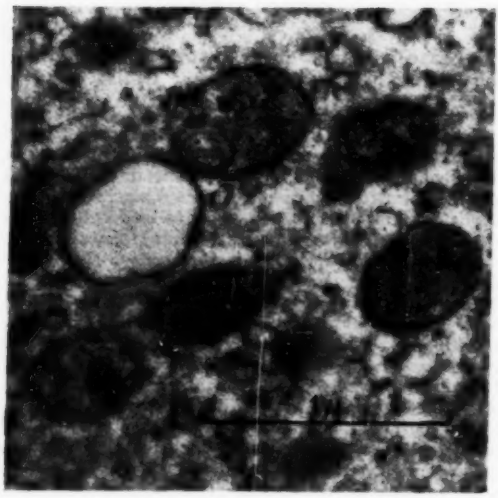

Fig. 1. Dense cytoplasmic bodies in an irradiation giant cell after 1 hr. in a medium containing 'Thorotrast'. The structures have internal membranes and contain granules of thorium dioxide

is prevented by radiation, the dense cytoplasmic bodies increase in number. The build-up of these structures, possibly with a high enzyme content, may be a factor in the death of these cells. The greater concentration of 'Thorotrast' in the dense bodies of the giant cells suggests that the rate of pinocytosis is greater than in the normal cells. Such a change could be correlated with the increased volume of the cell and the relatively decreased surface area available for the diffusion of nutrients.

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MICROBIOLOGY

Incorporation of Molecular Oxygen during Microbial Utilization of Olefins

The utilization of various alkanes by certain bacteria involves the incorporation of molecular oxygen into the conversion products[1] and into the bacterial cells[2]. The attack of the olefin 1-hexadecene at the saturated end of the molecule[3] probably is not different from that of the alkanes. Instances where the oxidative attack occurs at the double bond in olefins[3,4] have now been examined with the use of oxygen-18. Also, the cells of an ethylene-utilizing bacterium were analysed similarly.

The yeast *Candida lipolytica* A.T.C.C. 8661 was incubated at 30° C. for 4 days with continuous shaking in a closed 4-litre flask containing 800 ml. of the mineral salts solution of Bruyn[4], supplemented with 30 ml. of 1-hexadecene or 1-octadecene. The gas phase contained 80 per cent of labelled oxygen. The culture was extracted with diethyl ether. Chloroform was added to dissolve the diol crystals in the extracted unutilized olefin and the diols were purified by column chromatography[5]. The diols were recrystallized twice from *n*-hexane and dried *in vacuo* over phosphorus pentoxide (Table 1).

Table 1

	Hexadecane-1,2-diol	Octadecane-1,2-diol
Substrate	1-hexadecene	1-octadecene
Yield of recrystallized product	32·5 mgm.	70·6 mgm.
Melting point	85° C.	86·5° C.
Bromine test for double bond (ref. 6)	Negative	Negative
Periodate test for diol (ref. 7)	Positive	Positive
Purity, by periodate titration (ref. 8)	97·2 per cent	96·0 per cent
Analysis, found	C, 73·91 per cent; H, 12·75 per cent	75·12 per cent; H, 12·91 per cent
theory	C, 74·4 per cent; H, 13·2 per cent	75·4 per cent; H, 13·2 per cent
Formaldehyde produced by periodate oxidation (ref. 9)	Positive	Positive

The *Candida* cells from the octadecene culture were also analysed for oxygen-18. Cells of the 'ethylene bacterium' were recovered from mineral-salts medium in an atmosphere containing 10 per cent ethylene and 30 per cent of labelled oxygen. Cells of this bacterium were also obtained under comparable conditions with 1 per cent sodium acetate instead of the ethylene.

Isotopic composition of the products was determined by established procedures[10,11] (Table 2).

Table 2

Product	Substrate	Atom percentage excess ^{18}O		Percentage of oxygen in product derived from O
		O_2	Product	
Hexadecane-1,2-diol	1-Hexadecene	2·66	1·50	56·4
Octadecane-1,2-diol	1-Octadecene	5·47	1·69	31·0
Octadecane-1,2-diol	1-Octadecene	5·50	1·62	29·6*
Octadecane-1,2-diol	1-Octadecene	5·50	1·99	36·2*
Candida lipolytica cells	1-Octadecene	5·50	0·057	1·04
'Ethylene bacterium' cells	Ethylene	5·02	0·194	3·67*
'Ethylene bacterium' cells	Ethylene	5·02	0·164	3·27*
'Ethylene bacterium' cells	Ethylene	4·62	0·075	1·62
'Ethylene bacterium' cells	Sodium acetate	5·36	0·006	0·11

* Duplicate flasks in the same experiment. The orange-yellow pigmented ethylene bacterium was isolated from soil. It is a Gram-positive, aerobic, motile, non-sporulating rod. The minimal purity of the ethylene used in these experiments was 99 mole per cent.

Although a large fraction of the diol oxygen was derived from molecular oxygen, the results do not show whether one or both oxygen atoms of the diols came from the atmosphere. Assuming that the oxygen in any one position in the diol molecule was introduced by only one mechanism, the minimal theoretical value for incorporation is 50 per cent. The decidedly lower values for octadecane-1,2-diol in all probability indicate that an exchange had taken place whereby the oxygen-18 originally incorporated was partially replaced by oxygen-16 derived from water. The value of 56·4 per cent in the case of hexadecane-1,2-diol suggests that both oxygen atoms were derived initially from the atmosphere, but better evidence is required.

The cells of *Candida lipolytica* were also enriched in oxygen-18, as expected[2] from the assimilation of labelled intermediate diol. The 15- to 35-fold enrichment in oxygen-18 of the bacterial cells grown on ethylene over those grown on sodium acetate is indicative of an incorporation of molecular oxygen in the primary attack on the ethylene. By analogy, these results may be taken to imply, but not prove, that oxidation of ethylene by this bacterium takes place via ethylene glycol formed by the incorporation of molecular oxygen. Ethylene glycol was shown to serve as a sole source of carbon and energy for the 'ethylene bacterium'.

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Antigenic Structure of *Entamœba histolytica*

IMMUNOLOGICAL investigations on the specific antigens of *Entamœba histolytica* are complicated by the presence of concomitant bacterial flora in the culture. The precipitin reaction in cases of clinical amœbiasis has been investigated[1,2]. Menendez[3] reported the presence of precipitin antibodies in the serum of rabbit immunized with cultures of *Entamœba histolytica*. In the present work the precipitating antigens of these parasites were analysed by agar-gel diffusion and intragel absorption techniques.

Entamœba histolytica, strain *E.H.* 1, was used in this work. The associated bacterial flora in the culture were *Escherichia coli* and *Pseudomonas pyocyaneus*. *Ent. histolytica* grown in Row's hæmoglobin media at 37° C. for 48 hr. was treated with dihydrostreptomycin sulphate to kill the bacteria. In each test, materials from thirty culture tubes were pooled and centrifuged at 2,000 r.p.m. for 5 min. The supernatant fluid was discarded and the deposit was re-suspended in Ringer's solution so as to contain about 100–150 parasites/low-power field. Sera of rabbits hyperimmunized with cultures of *Ent. histolytica* were used and are referred to as 'antiamœba' sera in this communication. Sera were also cultivated against *E. coli* and *Ps. pyocyaneus*.

Diffusion of antigen and antibody in agar gel was carried out according to the method of Feinberg[4] as adapted by Ghosh and Mukerjee[5]. In order to eliminate the reactions due to the antigens of associate bacteria, controls were set up with *E. coli* and *Ps. pyocyaneus* antigens in each test. It can be seen in Fig. 1*a* that 'antiamœba' serum gave rise to three precipitin bands against *E. coli* and two bands against *Ps. pyocyaneus* antigens. But when the amœba culture was used, a number of bands appeared between the antigen and antiserum wells and it was not possible to delineate the specific bands of amœbæ. This was due to the presence of antibodies against *E. coli* and *Ps. pyocyaneus* in the 'antiamœba' serum and the corresponding antigens in the antigenic preparations of amœba. By incorporation of 50 per cent (v/v) anti*coli* and anti*pyocyaneus* sera in the media, it was possible to absorb the bacterial antigens and identify the three specific precipitin bands of amœbæ.

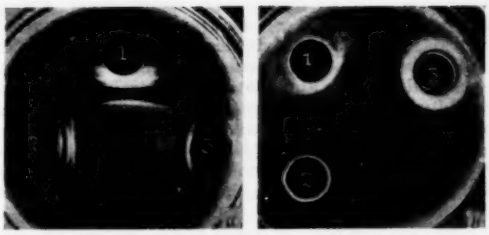

Fig. 1. *a*, Central well; antiamœba serum; 1, amœba antigen; 2, *E. coli* antigen; 3, *Ps. pyocyaneus* antigen. *b*, Intragel specific absorption 50 per cent anti*coli* and anti*pyocyaneus* sera (v/v) in gel. Arrangements of the wells are the same as in Fig. 1*a*. Note unmasking of three specific bands of amœba

On adding 'antiamœba' serum to the media all the bands, including those due to *Ent. histolytica*, were eliminated.

Since the rabbit's blood was used both for the preparation of Row's hæmoglobin media and as the source of antisera, no precipitin band appeared against media controls.

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GENETICS

Skewed Recombination in a Rare Interspecific Jute Hybrid

Islam and Rashid[1] and Swaminathan *et al.*[2] have recently described the morphological and cytological characteristics of the F_1 hybrids between the two cultivated jute species, *Corchorus olitorius* L. and *C. capsularis* L. The F_1 plants studied were intermediate in phenotype, but an interesting genetic situation was found when we examined the F_2 and F_3 generations of two hybrids of *C. olitorius* (♀) × *C.*

capsularis (♂). Chromosome associations during microsporogenesis were analysed in the two F_1 hybrids, and five bivalents and one quadrivalent, or one trivalent and a univalent, occurred in several cells at diakinesis and metaphase I (ref. 2). One of the bivalents was heteromorphic. The F_2 progenies of these two hybrids contained more than 40 per cent of non-viable seedlings. Also, about 11 per cent of the F_2 population had various types of chlorophyll deficiency, abnormalities in leaf shape and poor vigour.

The varieties of *C. olitorius* and *C. capsularis* used in this work differed prominently from each other in branching habit, leaf index, flower size, number of stamens, size and shape of capsules, and seed colour. The F_2 population of one cross, comprising 138 individuals, was analysed for these characters according to the hybrid index procedure of Anderson[3]. The results (Fig. 1) show that there is a preponderance in the population of plants with an index value approaching that for *C. olitorius*. While a wide range of segregation was observed for the shape and size of capsule, no plant had the *capsularis* type of globose fruit.

Chromosome associations were studied in seven F_2 plants, and differential segments and inversion loops at pachytene, a heteromorphic bivalent at metaphase I, and a dicentric bridge and an acentric fragment at anaphase I were recorded. Two plants proved to be trisomics with $2n = 15$ and in both of them the capsules occurred in clusters of 5–7 as in the *capsularis* parent (Fig. 2), thereby indicating that the extra chromosome may be a *capsularis* one carrying the gene for this trait. In the F_2 population raised from one of the hybrids, phenotypic segregation was even more prominently skewed in the direction of *olitorius* than in the F_2.

The cytological results, the occurrence of a high proportion of unthrifty and non-viable seedlings and the skewed segregation behaviour observed in F_2 and F_3 progenies indicate that the genomes of *C. olitorius* and *C. capsularis* have differentiated in the direction of increased coherence[4], which automatically decreases the possibility for effective recombination. It has not been possible, so far, to make this cross with *C. capsularis* as the pistillate parent. Whether or not cytoplasmic factors have any role in determining coherence and the direction of skewness in segregation can be ascertained only when the reciprocal hybrid becomes available. From the point of view of breeding, the occurrence of trisomics in the hybrid progenies is a useful feature, since a way is thus open for substituting whole pairs of chromosomes that cohere but do not recombine.

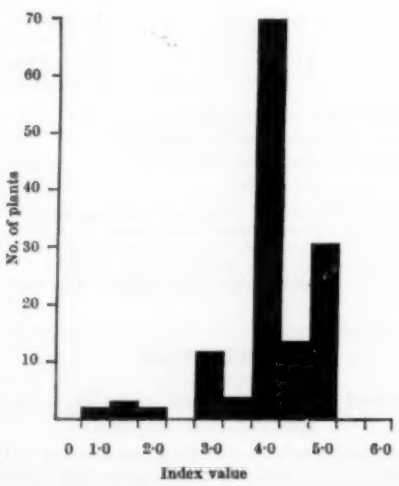

Fig. 1. Histogram showing the number of F_2 plants under each index value in the cross *C. olitorius* × *C. capsularis*. The population was scored for six different morphological characters and to each character typical of *C. olitorius* an index number of 1 was assigned. Thus plants totally like *C. capsularis* will have an index value of 0 and those like *C. olitorius* will have a value of 6. A value of 0·5 was given when the phenotype for a character was intermediate between that of the parents

Fig. 2. Fruiting branches of (left to right), *C. olitorius* (♀), the trisomic F_2 with bunched capsules and *C. capsularis* (♂). 3/8 nat. size

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Hæmoglobin Polymorphism in Fishes

Meristic and morphometric characters have been the most commonly used traits in the investigation of races or sub-populations of fishes. The differences in such characters among various populations may be due to variation in genetic as well as environmental factors. However, the relative influence of these two factors is usually unknown[1]. Consequently, it would be advantageous to use gene-frequency data based on Mendelian characters, the expression of which may be considered not to be influenced by environmental variation.

In mammals, especially man, this has been successfully done with blood types and hæmoglobin types[2,3]. Variation of blood-groups within fish species has been described by several authors[4–8]. Although zone electrophoresis of fish hæmoglobins has been reported by Buhler and Shanks[9] and by Chandrasekhar[10],

Fig. 1. Hæmoglobin patterns of whiting. 1, Type Hb I-1; 2, type Hb I-1-2; 3, type Hb I-2

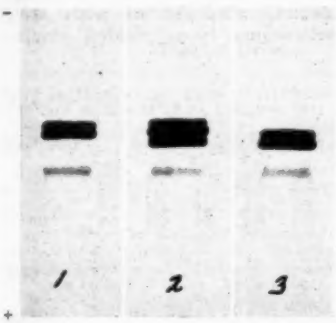

Fig. 2. Hæmoglobin patterns of cod. 1, Type Hb I-1; 2, type Hb I-1-2; 3, type Hb I-2

no intraspecific variation in electrophoretic mobilities was detected.

This communication describes hæmoglobin polymorphism in two species of fish, namely, whiting and cod. Polymorphism was detected by a modification of the agar electrophoresis technique described by Giri[11]. The present experiments were carried out with phosphate buffer (*p*H 7·3, ionic strength 0·02). Only freshly prepared oxyhæmoglobin solutions have been used.

In whiting (*Gadus merlangus*) three different electrophoretic patterns were found (Fig. 1). The whiting hæmoglobins were run at room temperature for 30 min. at 200 V. between electrodes. The patterns all have a slow-moving component (Hb II) in common. In addition, they may have either one or both of two faster-moving components (HbI–1 and HbI–2). The three types of individuals are called type Hb I–1, type Hb I–1–2, and type Hb I–2. Both in type Hb I–1 and in type Hb I–1–2 the Hb I–1 component is accompanied closely at the cathodic side by a weak minor component. No correlation of hæmoglobin type with sex or size of the specimen could be detected.

Apart from the common Hb II component the situation observed here is similar to the hæmoglobin polymorphism described in man, cattle and sheep. In these species, the underlying genetics have been elucidated[2]. By analogy a genetic hypothesis involving two alleles may be tentatively adopted to explain the genetics of the hæmoglobin variation observed in whiting. According to this hypothesis two co-dominant allelic genes Hb I^1 and Hb I^2 determine the hæmoglobin components Hb I–1 and Hb I–2 respectively. Type Hb I–1 and type Hb I–2 are considered as homozygous for the corresponding allele, and type Hb I–1–2 would represent the heterozygote. This hypothesis receives some support from the fact that the distribution of the supposed genotypes is consistent with the distribution calculated according to the Hardy–Weinberg law (Table 1). There is no significant heterogeneity between the samples represented in Table 1.

In cod (*Gadus morrhua*) three distinct patterns were again observed (Fig. 2). The hæmoglobin components of cod require longer time and cooling of the apparatus for their resolution. They were run for 60 min. at 200 V. between electrodes. It should be noted that although the same designations (Hb I–1, Hb I–2, and Hb II) have been used for cod and whiting hæmoglobin components, it is not known whether the two species have any component in common.

Both the Hb I–1 and the Hb I–2 component of cod hæmoglobin are accompanied at the cathodic side, by a minor component, Hb I–1′ and Hb I–2′ respectively. The Hb I–2′ component was inseparable from the Hb I–1 component in the supposed heterozygote as well as in an *in vitro* mixture of hæmoglobin from individuals of type Hb I–1 and Hb I–2. This situation is similar to that described for serum transferrin types in mice[12]. Since storing the cod hæmoglobin solutions tends to increase the relative amount of minor components, they may represent denaturation products.

A two-allele genetic hypothesis may also be adopted to explain the findings with cod. The results obtained are presented in Table 2. A highly significant difference in gene frequencies can be seen between the Bornholm sample and the three other samples. Apart from the Bornholm material the samples are consistent with the Hardy–Weinberg distribution and show similar gene frequencies. The poor fit ($P = 0{\cdot}0004$) of the Bornholm sample is most easily explained by assuming that it represents a population homozygous or nearly homozygous for the Hb I^2 allele with some admixture of migrants from a population having gene frequencies similar to those

Table 1. Distribution of Hæmoglobin Types in Samples of Whiting from Different Areas

Type Supposed genotype	HbI–1 HbI^1/HbI^1	HbI–1–2 HbI^1/HbI^2	HbI–2 HbI^2/HbI^2	Total	Frequency of HbI^1 allele
Inner Danish Waters (Kattegat, The Sound, and Fehmarn Belt)	16	78	72	166	0·33
Southern North Sea (near Holland)	10	40	46	96	0·31
Northern North Sea (near Aberdeen)	10	21	21	52	0·39
Irish Sea	4	18	16	38	0·34
Totals observed	40	157	155	352	0·34
Totals expected according to the Hardy–Weinberg law	39·9	157·2	154·9		

Table 2. Distribution of Hæmoglobin Types observed in Samples of Cod from Different Areas compared with the Distribution expected according to the Hardy–Weinberg Law of Genotype Frequencies

Type Supposed genotype		HbI–1 HbI^1/HbI^1	HbI–1–2 HbI^1/HbI^2	HbI–2 HbI^2/HbI^2	Total	Frequency of HbI^1 allele
The Sound	observed	93	112	37	242	0·62
	expected	91·7	114·6	35·7		
Fehmarn Belt	observed	27	30	12	69	0·61
	expected	25·6	32·8	10·6		
Great Belt	observed	37	50	15	102	0·61
	expected	37·7	48·6	15·7		
Baltic Sea, near Rønne, Bornholm	observed	2	2	74	78	0·04
	expected	0·1	5·8	72·1		

observed in the Sound and Fehmarn Belt. This interpretation, although supported by results from Danish tagging experiments[12], should be tested by further investigation.

In addition to cod and whiting, distinct intraspecific variation in hæmoglobin patterns has been observed in sole (*Solea solea*) and eel-pout (*Zoarces viviparus*). These preliminary results suggest that hæmoglobin polymorphism may be of rather common occurrence in fishes and that zone electrophoresis of hæmoglobins may become a valuable tool in taxonomic investigations of fishes at the sub-specific level.

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VIROLOGY

Inactivation of Rous Virus by Phospholipase *A*

Rous virus is known to consist of protein, ribonucleic acid (RNA) and lipid, about 40 per cent of which is in the form of phospholipids[1,2]. Partially purified preparations of the virus are inactivated by a wide range of lipid solvents—organic solvents, bile salts and synthetic detergents—and the loss of infectivity is associated with the shedding from the virus particles of protein-like material[3].

Anderson and Ada[4] have shown that Murray encephalitis virus—an arthropod-borne virus containing RNA, protein and lipid—is inactivated by phospholipase *A*. This communication reports a similar loss of infectivity in Rous virus preparations incubated with phospholipase *A*.

Partially purified Rous virus suspensions were made from fresh fowl-grown tumours according to the method of Carr and Harris[5] as modified by Bather[6]. Phospholipase *A*, supplied by Miss H. Doery of the Commonwealth Serum Laboratories, had been purified from the venom of the black snake (*Pseudechis porphyriacus*). The concentration of enzyme used in these experiments was 100 μgm. per ml. of 0·9 per cent sodium chloride ; each sample was boiled for 10 min. to ensure that phospholipase *A* was the only functional enzyme present.

Equal volumes of virus suspension (in phosphate-citric buffer *p*H 7·2) and phospholipase *A* were mixed and incubated at 37° C. for 30 min. As a control, the virus suspension was mixed in 0·9 per cent sodium chloride and kept at the same temperature and for the same time as the experimental tubes. The infectivity of the control and treated samples was estimated by titration in young chicks[5].

Table 1 shows the loss of infectivity which resulted from the incubation of Rous virus with phospholipase *A* in two experiments. Experiments with MH_2 tumour virus preparations have yielded similar results (Table 2).

Table 1. Effect on Infectivity of Rous Virus incubated with Phospholipase *A* (100 μgm./ml.) at 37° C. for 30 min.

		Dilution of sample and No. of tumours/No. of chicks inoculated at each dilution							Infectivity
		10	10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	
1	Control	2/2	2/2	4/4	4/4	4/4	4/4	0/4	$10^{5.5}$
	Treated	2/2	2/2	0/2	0/4	0/4	0/4	0/4	10^{1}
2	Control	2/2	2/2	2/2	4/4	4/4	4/4	4/4	$>10^{6}$
	Treated	2/2	1/2	0/2	0/4	0/4	0/4	0/4	10^{1}

Table 2. Effect on Infectivity of MH_2 Virus incubated with Phospholipase *A* (100 μgm./ml.) at 37° C. for 30 min.

		Dilution of sample and No. of tumours/No. of chicks inoculated at each dilution							Infectivity
		10	10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	
1	Control	1/2	2/2	2/2	4/4	4/4	1/4	0/4	$10^{4.7}$
	Treated	0/2	0/2	0/2	0/4	0/4	0/4	0/4	0
2	Control	2/2	2/2	4/4	4/4	2/4	0/4	0/4	$10^{4.5}$
	Treated	0/2	0/2	0/4	0/4	0/4	—	—	0

Since phospholipase *A* splits specifically only fatty acids bound in the − position, it was concluded from these results that Rous virus (and probably the other fowl tumour viruses as well) are inactivated by the cleavage of fatty acids from phospholipids contained in their structure.

This result would support a previous suggestion[3] that the integrity of at least some of the protein bound to the phospholipid moiety in the extranucleoid region of Rous virus particles is essential for infectivity. It may be that disruption of this phospholipid-protein wrapping is so radical as to cause irreversible injury to the virus RNA, and that it is this secondary effect which destroys the reproductive capacity of the virus. On the other hand, the lipoprotein shell of Rous virus may allow the virus particles to react with some intracellular system and this 'acceptance' may be a necessary prerequisite for virus replication.

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[1] Claude, A., *J. Exp. Med.*, **61**, 41 (1935).
[2] Bather, R., *Brit. J. Cancer*, **11**, 611 (1957).
[3] Drayton, H. A., *Brit. J. Cancer*, **15** (2), 348 (1961).
[4] Anderson, S. G., and Ada, G. L., *Nature*, **188**, 876 (1960).
[5] Carr, J. G., and Harris, R. J. C., *Brit. J. Cancer*, **5**, 83 (1951).
[6] Bather, R., *Brit. J. Cancer*, **7**, 492 (1953).

FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, December 4

INSTITUTE OF METAL FINISHING (in the Gower Room, Hotel Russell, London, W.C.1), at 3.30 p.m.—Dr. G. L. J. Bailey: "The Changing Face" (Presidential Address).

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London, Ducane Road, London, W.12), at 4 p.m.—Dr. H. E. Huxley: "Mechanism of Muscular Contraction".*

INSTITUTION OF ELECTRICAL ENGINEERS, ELECTRONICS AND COMMUNICATIONS SECTION (at Savoy Place, London, W.C.2, at 5.30 p.m. Discussion on "Backward Waves in Waveguides", opened by Dr. P. J. B. Clarricoats, Mr. R. A. Waldron and Mr. G. H. B. Thompson.

INSTITUTION OF MECHANICAL ENGINEERS, APPLIED MECHANICS, THEORY OF MATERIALS OF CONSTRUCTION GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Discussion on "Can Plastic Components be Designed Rationally?"

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 6 p.m.—Prof. W. K. Estes (Indiana): "Current Foci of Research in Mathematical Behaviour Theory".* (Further lectures on December 7 and 11.)

SOCIETY OF CHEMICAL INDUSTRY, LONDON SECTION (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Scientific Film Evening.

Tuesday, December 5

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 1.15 p.m.—Dr. H. Kalmus: "Biological Time-keeping".*

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Prof. L. F. Bates, F.R.S.: "Domains and Domain Patterns".

PARLIAMENTARY AND SCIENTIFIC COMMITTEE, GENERAL COMMITTEE (in Committee Room 12, House of Commons, London, S.W.1), at 5.30 p.m.—Dr. D. W. Hill and Sir Charles Goodeve, F.R.S.: "The Developing and Financing of Research Associations".

ROYAL SOCIETY OF MEDICINE, PATHOLOGY SECTION (at 1 Wimpole Street, London, W.1), at 5.30 p.m.—Symposium "On Histochemistry and Cytochemistry". Speakers: Dr. N. M. Hancox, Mr. S. J. Holt and Mr. A. J. Hale.

UNIVERSITY OF LONDON (at Imperial College of Science and Technology, London, S.W.7), at 5.30 p.m.—Prof. M. G. Fleming: Inaugural Lecture.

INSTITUTION OF POLISH ENGINEERS IN GREAT BRITAIN, GROUP FOR ECONOMIC, SOCIAL AND MANAGEMENT STUDIES (at 55 Princes Gate, Exhibition Road, London, S.W.7), at 7 p.m.—Mr. E. A. Cooper-Key: "Management Training in the Armed Forces and in Industry".

ROYAL PHOTOGRAPHIC SOCIETY OF GREAT BRITAIN (at 16 Princes Gate, London, S.W.7), at 7 p.m.—Dr. R. G. W. Ollerenshaw: "Design for Projection: a Study of Legibility" (Eleventh Renwick Memorial Lecture).

SCIENCE FORUM (at Friends House, Euston Road, London, N.W.1), at 7.30 p.m.—Dame Kathleen Lonsdale, F.R.S.: "Statistical Ethics".

Wednesday, December 6

INSTITUTE OF PHYSICS AND PHYSICAL SOCIETY, COLOUR GROUP (at the Northampton College of Advanced Technology, St. John Street, London, E.C.1), at 3 p.m.—Dr. B. H. Crawford: "Colour Matching and Visual Adaptation".

INSTITUTION OF AGRICULTURAL ENGINEERS (at Cromwell Hall, Earls Court, London), at 4 p.m.—Dr. A. H. Willis: "Agricultural Engineering Problems in Australia".

ROYAL STATISTICAL SOCIETY (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5 p.m.—Prof. C. R. Rao: "Efficient Estimates and Optimum Inference Procedures in Large Samples".

INSTITUTE OF BIOLOGY (in the Lecture Theatre of the British Museum (Natural History), Cromwell Road, London, S.W.7), at 5.15 p.m.—Dr. J. M. Tanner: "Human Growth in its Comparative and Evolutionary Aspects" (Second Darwin Lecture).

INSTITUTE OF PETROLEUM (at 61 New Cavendish Street, London, W.1), at 5.30 p.m.—Dr. J. A. Carruthers and Mr. K. J. Marsh: "Charge Relaxation in Hydrocarbon Liquids flowing through Conducting and Non-conducting Pipes"; Mr. K. J. Wigley and Dr. J. A. Carruthers: "The Estimation of Electrostatic Potentials, Fields, and Energies in a Rectangular Metal Tank containing Charged Fuel".

BRITISH INSTITUTION OF RADIO ENGINEERS, COMPUTER AND MEDICAL ELECTRONICS GROUPS (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6 p.m.—Discussion on "Possible Uses of Computers in Medical Diagnosis" opened by Dr. A. D. Booth.

INSTITUTION OF ELECTRICAL ENGINEERS, EDUCATION DISCUSSION CIRCLE (at Savoy Place, London, W.C.2), at 6 p.m.—Discussion on "Teaching Protective Systems" opened by Mr. G. Heywood.

Wednesday, December 6—Friday, December 8

ROYAL PHOTOGRAPHIC SOCIETY OF GREAT BRITAIN, SCIENTIFIC AND TECHNICAL GROUP (at the Royal Society of Arts, John Adam Street, Adelphi, London, W.C.2), at 9.30 a.m. daily—Symposium "Document Copying by Photography".

Thursday, December 7

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Sir Gavin De Beer, F.R.S.: "The Origins of Darwin's Ideas on Evolution and Natural Selection" (The Wilkins Lecture).

INSTITUTE OF REFRIGERATION (at the Institute of Marine Engineers, The Memorial Building, 76 Mark Lane, London, E.C.3), at 5.30 p.m.—Dr. J. C. Fidler: "Developments in Storage of Fruits".

INSTITUTION OF ELECTRICAL ENGINEERS (at Savoy Place, London, W.C.2), at 5.30 p.m.—Prof. M. W. Thring: "Magnetohydrodynamics" (Parsons Memorial Lecture).

ROYAL INSTITUTION, LIBRARY CIRCLE (at 21 Albemarle Street, London, W.1), at 5.30 p.m.—Mr. K. D. Vernon: "Forgotten Worthies of the Royal Institution. 2: William Savage and Thomas Webster".

ROYAL METEOROLOGICAL SOCIETY (in the Conference Hall, County Hall, London, S.E.1), at 5.30 p.m.—Mr. C. E. Wallington: "Meteorology and Gliding".

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. F. Kingsley Sanders: "Infective Nucleic Acids and Virus Synthesis".* (Sixteenth of seventeen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

OIL AND COLOUR CHEMISTS' ASSOCIATION, LONDON SECTION (at the Royal Society of Tropical Medicine and Hygiene, Manson House, 26 Portland Place, London, W.1), at 7 p.m.—Mr. A. Macmaster: "Aircraft Paints".

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (at the Northampton College of Advanced Technology, St. John's Street, London, E.C.1), at 7 p.m.—Mr. T. M. Dunn: "Ultra-violet Spectroscopy".

Thursday, December 7—Friday, December 8

POWDER METALLURGY JOINT GROUP of the IRON AND STEEL INSTITUTE and the INSTITUTE OF METALS (at Church House, Great Smith Street, London, S.W.1), at 2.30 p.m. on Thursday and 10 a.m. on Friday—Winter Meeting.

Friday, December 8

ASSOCIATION OF APPLIED BIOLOGISTS (at the British Museum (Natural History), South Kensington, London, S.W.7), at 10.50 a.m.—Paper reading meeting.

INSTITUTION OF ELECTRICAL ENGINEERS, MEDICAL ELECTRONICS DISCUSSION GROUP (at Savoy Place, London, W.C.2), at 6 p.m.—Discussion on "The Peltier, Hall and Seebeck Effects".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Dame Kathleen Lonsdale, F.R.S.: "Restless Atoms in Solids".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

SENIOR DEMONSTRATOR (with a degree with biochemistry as a major subject and preferably some teaching or postgraduate experience) IN BIOCHEMISTRY at the University of Melbourne, Australia—The Secretary, Association of Universities of the British Commonwealth (Branch Office), Marlborough House, Pall Mall, London, S.W.1 (Australia and London, December 15).

LECTURER (with an honours degree with special interest in inorganic and/or physical chemistry, and preferably experience in university teaching) IN CHEMISTRY at the University College of Townsville, University of Queensland—The Secretary, Association of Universities of the British Commonwealth (Branch Office), Marlborough House, Pall Mall, London, S.W.1 (December 16).

EXPERIMENTAL OFFICER or SENIOR EXPERIMENTAL OFFICER (with Higher National Certificate, degree or similar qualification) IN THE DEPARTMENT OF ELECTRICAL ENGINEERING—The Registrar, The University, Manchester 13 (December 18).

ORGANIC CHEMIST or BIOCHEMIST (with a good honours degree or equivalent qualification), for research in structural carbohydrate chemistry and immunochemistry—The Secretary, Lister Institute of Preventive Medicine, Chelsea Bridge Road, London, S.W.1 (December 30).

LECTURER IN GEOGRAPHY; a LECTURER IN PHYSICS; and a LECTURER IN PSYCHOLOGY at the University of Tasmania—The Secretary, Association of Universities of the British Commonwealth (Branch Office), Marlborough House, Pall Mall, London, S.W.1 (Australia and London, December 31).

LECTURER (medical graduate of at least two years standing with experience in teaching and research) IN ANATOMY—The Secretary, The Medical College of St. Bartholomew's Hospital, West Smithfield, London, E.C.1 (December 31).

OFFICIAL FELLOWS (2) IN PHYSICS, to carry responsibility for the teaching of theoretical and experimental physics—The Warden, Wadham College, Oxford (December 31).

ASSISTANT IN THE SUB-DEPARTMENT OF PHARMACOLOGY, University College of The West Indies, for duties which include research, demonstration and some teaching for M.B., B.S., degrees of London University—The Secretary, Senate Committee on Colleges Overseas in Special Relation, University of London, Senate House, London, W.C.1 (January 1).

LECTURERS OR ASSISTANT LECTURERS (2) (with a major interest in the theory of machines, and preferably an interest in metallurgy, machine design or engineering drawing) IN MECHANICAL ENGINEERING at the University College of The West Indies—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (January 1).

LECTURER OR ASSISTANT (preferably with a special interest in solid state physics) IN PHYSICS—The Secretary, Queen's College (University of St. Andrews), Dundee (January 8).

TECHNICIANS (2) IN THE DEPARTMENT OF ANATOMY, Makerere University College, East Africa—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (January 10).

CHAIR OF ANATOMY in the University of Malaya, Singapore—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (January 15).

CHAIRS (4) IN ENGINEERING in Monash University, Melbourne—The Secretary, Association of Universities of the British Commonwealth (Branch Office), Marlborough House, Pall Mall, London, S.W.1, or The Registrar, Monash University, P.O. Box 92, Clayton, Victoria, Australia (Australia and London, January 31).

SENIOR LECTURER (with an appropriate science qualification and wide experience of clinical biochemistry) IN CLINICAL BIOCHEMISTRY at the University of Otago, Dunedin, New Zealand—The Secretary, Association of Universities of the British Commonwealth (Branch Office), Marlborough House, Pall Mall, London, S.W.1 (New Zealand and London, January 31).

OFFICIAL FELLOW AND TUTOR IN PHYSICS, or a LECTURER IN PHYSICS—The Principal, St. Hugh's College, Oxford (February 1).

IMPERIAL CHEMICAL INDUSTRIES RESEARCH FELLOWS IN CHEMISTRY, PHYSICS, METALLURGY, ENGINEERING, GEOLOGY, AGRICULTURAL SCIENCE or related subjects—The Registrar, University of Wales, University Registry, Cathays Park, Cardiff (March 5).

ASSISTANT (graduate in astronomy, or in physics or electrical engineering (electronics) with some training or interest in astronomy) TO THE DIRECTOR OF THE JEREMIAH HORROCKS AND WILFRED HALL OBSERVATORIES—Chief Education Officer, Municipal Building, Preston.

ASSISTANT PROFESSOR (with a Ph.D. in pharmacology); and an ASSISTANT PROFESSOR (with a Ph.D. in pharmacognosy or plant chemistry)—Prof. J. R. Murray, Director of the School of Pharmacy, University of Manitoba, Winnipeg, Canada.

BIOCHEMIST for fundamental research on collagen and gelatin—The Director of Research, British Gelatine and Glue Research Association, 2a Dalmeny Avenue, Holloway, London, N.7.

CHIEF LABORATORY TECHNICIAN—Head, Applied Physics Department, Northampton College of Advanced Technology, St. John Street, London. E.C.1.

LECTURERS, ASSISTANT PROFESSORS, and ASSOCIATE PROFESSORS IN THE DEPARTMENT OF MATHEMATICS (Edmonton campus or Calgary campus)—Prof. M. Wyman, Mathematics Department, University of Alberta, Edmonton, Alberta, Canada.

LECTURERS (with a first- or second-class honours degree in mathematics, physics and most branches of engineering), to teach students for the B.Sc. degrees of London University—The Registrar, Royal Military College of Science, Shrivenham, near Swindon, Wilts.

LIBRARIAN (with a knowledge of chemistry or physics) IN THE DEPARTMENT OF CHEMICAL ENGINEERING AND CHEMICAL TECHNOLOGY—Head of the Department of Chemical Engineering and Chemical Technology, Imperial College of Science and Technology, London, S.W.7.

NATIONAL COAL BOARD RESEARCH ASSISTANT (good honours graduate or equivalent) IN THE DEPARTMENT OF PURE AND APPLIED CHEMISTRY, to continue a study on the origin of coal tar components—The Reader in Industrial Chemistry, Northampton College of Advanced Technology, St. John Street, London, E.C.1.

RESEARCH ASSISTANT (with a good honours degree, or its equivalent, in physiology, biochemistry or zoology, and preferably experience in some field of hormone research or immunochemistry) IN THE PHYSIOLOGY DEPARTMENT, to study the physiology of prolactin with special reference to its assay in body fluids—The Secretary, National Institute for Research in Dairying (University of Reading), Shinfield, Reading, quoting Ref. 61/31.

RESEARCH ASSISTANT (with experience of numerical analysis and the writing of computer programmes) IN THE MATHEMATICS DEPARTMENT—The Registrar, Brunel College of Technology, Woodlands Avenue, Acton, London, W.3.

SENIOR LABORATORY TECHNICIAN IN THE BACTERIOLOGY DEPARTMENT, Connaught Hospital, Walthamstow, London, E.17—The Secretary, Forest Group H.M.C., Langthorne Road, Leytonstone, London, E.11.

SENIOR LECTURER IN PHYSICS, and a LECTURER IN PHYSICS—Clerk to the Governing Body, Northern Polytechnic, Holloway, London, N.7.

SENIOR RESEARCH ASSISTANT (preferably with some research experience) IN THE DEPARTMENT OF PHYSICS, for a programme of work on the magnetic properties of thin films, provisionally for one year in the first instance—The Principal, Royal Holloway College (University of London), Englefield Green, Surrey.

TECHNICIAN or JUNIOR TECHNICAL OFFICER (female, preferably with "A" level G.C.E. or equivalent), to assist in biological research at Pollards Wood Research Station, Chalfont St. Giles, Bucks—The Secretary, Institute of Cancer Research, 33 Sumner Place, London, S.W.7, quoting Ref. 301/B/83.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

British Medical Bulletin, Vol. 17, No. 3 (September, 1961): Human Genetics. Pp. 177–264+xv. (London: British Council, 1961.) 20s. [59

Wye College (University of London). Annual Report of the Department of Hop Research from 1st April, 1960, to 31st March, 1961. Pp. v+90+2 plates. Hop Research at Wye College in 1960. By H. S. Darling. Pp. 4. (Wye, Ashford: Wye College, University of London, 1961.) [79

Ministry of Agriculture, Fisheries and Food. Bulletin No. 148: Incubation and Hatchery Practice. By Dr. W. M. Allcroft. Pp. v+65+8 plates. (London: H.M. Stationery Office, 1961.) 5s. net. [79

Learning Theory and the Therapy of Neurosis. By R. Metzner. (*The British Journal of Psychology*, Monograph Supplements, No. 33.) Pp. v+29. (Cambridge: At the University Press, 1961.) 7s. 6d. net. [79

Department of Scientific and Industrial Research. National Engineering Laboratory Annual Report 1960: Report of the National Engineering Laboratory Steering Committee with the Report of the Director of the National Engineering Laboratory. Pp. iv+72+4 plates. (Edinburgh and London: H.M. Stationery Office, 1961.) 5s. net. [89

The Institute of Navigation. Report of the Council, 1960–61. Pp. 16. (London: Institute of Navigation, 1961.) [259

University of London. University College Calendar, 1961–62. Pp. lxi+504. (London: University College, 1961.) [259

Other Countries

New Zealand Forest Service: Forest Research Institute. Research Notes No. 25: The European House Borer *Hylotrupes bajulus* L., a Possible Pest for New Zealand. By R. H. Milligan. Pp. 19. (Wellington: Government Printer, 1961.) [79

Guide Book to the Royal Botanic Gardens, Melbourne. Pp. 28. (Melbourne: Royal Botanic Gardens, 1961.) 4s. (Australian). [89

United States Department of the Interior: Geological Survey. Water-Supply Paper 1501–A: Urban Growth and the Water Regimen. By John Savini and J. C. Kammerer. Pp. iv+43+1 plate. Professional Paper 402–A: Mechanism of Gravity Drainage and Its Relation to Specific Yield of Uniform Sands. By W. O. Smith. Pp. iii+12. 20 cents. Professional Paper 411–B: Transverse Diffusion in Saturated Isotropic Granular Media. By Akio Ogata. Pp. iii+8. 15 cents. (Washington, D.C.: Government Printing Office, 1961.) [89

Smithsonian Miscellaneous Collections. Vol. 143, No. 4: Comparison of Tektite Specimens from Empire, Georgia, and Martha's Vineyard, Massachusetts. By Roy S. Clarke, Jr., and Maxwell K. Carron. Pp. 1+18+6 plates. (Publication 4465.) (Washington, D.C.: Smithsonian Institution, 1961.) [89

Bulletin of the Museum of Comparative Zoology at Harvard College. Vol. 125, No. 3: Two Jurassic Turtle Skulls—a Morphological Study. By Thomas S. Parsons and Ernest E. Williams. Pp. 41–108+6 plates. (Cambridge, Mass.: Museum of Comparative Zoology at Harvard College, 1961.) [259

United States Department of Agriculture. Farmers' Bulletin No. 2168: Controlling Potato Insects. By W. A. Shands, B. J. Landis, and W. J. Reid, Jr. Pp. 16. (Washington, D.C.: Government Printing Office, 1961.) 10 cents. [259

Smithsonian Miscellaneous Collections. Vol. 142, No. 4: Cenozoic and Cretaceous Echinoids from Trinidad and Venezuela. By C. Wythe Cooke. Pp. 36+14 plates. (Publication 4459.) (Washington, D.C.: Smithsonian Institution, 1961.) [259

Work Half Done: Bernice P. Bishop Museum Annual Report for 1960. Pp. 30. (Honolulu, Hawaii: Bernice P. Bishop Museum, 1961.) [259

Institut Royal Météorologique de Belgique. Contribution No. 67: Etude des Propriétés Statistiques des plus Fortes Marées à Ostende (Belgique). Par Dr. R. Sneyers. Pp. 11. (Bruxelles: Institut Royal Météorologique de Belgique, 1961.) [259

Proceedings of the United States National Museum, Smithsonian Institution. Vol. 113, No. 3453: Notes on Australian Flies of the Family Conopidae. By Sidney Camras. Pp. 61–76. Vol. 113, No. 3454: New and Previously Known Millipeds of Panama. By H. F. Loomis. Pp. 77–124. Vol. 113, No. 3455: New General and New Species of Lacebugs from the Eastern Hemisphere (Hemiptera: Tingidae). By Carl J. Drake and Florence A. Ruhoff. Pp. 125–183. (Washington, D.C.: Government Printing Office, 1961.) [259

Museum of Comparative Zoology at Harvard College. Breviora. No. 138 (June 14, 1961): Pfeiffer's Unifigures Species of *Strophocheilus* (*Megalobulimus*). By T. E. Crowley and T. Pain. Pp. 8. No. 139, (June 15, 1961): A New Species of *Sphaerolaryngs* from Northern Haiti. By James D. Lazell. Pp. 5. No. 140, (June 27, 1961): A Preliminary Review of the Nearctic Species of *Sierolomorpha* (Hymenoptera). By Howard E. Evans. Pp. 12. No. 141, (June 28, 1961): Three New Toads from South America, *Bufo manicorensis*, *Bufo simulatus altiperuvianus*, and *Bufo quechua*. By José M. Gallardo. Pp. 8+3 plates. No. 142, (June 30, 1961): Australian Carabid Beetles VI—The Tropical and some Subtropical Species of *Pamborus*, *Mystropomus*, and *Nurus*. By P. J. Darlington, Jr. Pp. 13. Annual Report of the Director of the Museum of Comparative Zoology at Harvard College, 1959–1960. Pp. 29. (Cambridge, Mass.: Museum of Comparative Zoology at Harvard College, 1961.) [259

Bulletin of the Museum of Comparative Zoology at Harvard College. Vol. 125, No. 2: On the Major Arterial Canals in the Ear-Region of Testudinoid Turtles and the Classification of the Testudinoidea. By Samuel Booker McDowell, Jr. Pp. 21–38. (Cambridge, Mass.: Museum of Comparative Zoology at Harvard College, 1961.) [259

Proceedings of the California Academy of Sciences. Fourth Series. Vol. 30, No. 3, (August 31, 1961): Large Terebras (Mollusca) from the Eastern Pacific. By G. Dallas Hanna and Leo George Hertlein. Pp. 67–80+plates 6 and 7. Vol. 30, No. 4, (August 31, 1961): Four Species of Chitons from the Oanamic Province (Mollusca: Polyplacophora). By Allyn G. Smith. Pp. 81–90+plates 8 and 9. (San Francisco: California Academy of Sciences, 1961.) [259

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